"A COMPARATIVE STUDY OF SUXAMETHONIUM INDUCED MUSCLE FASCICULATIONS, POSTOPERATIVE MYALGIA AND HYPERKALEMIA WITH THE PRECURARIZATION AND SELF TAMING OF SUXAMETHONIUM."

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FOR

DOCTOR OF MEDICINE

(ANAESTHESIOLOGY)





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C E R T I F I C A T E

This is to certify that the work entitled, "A COMPARATIVE STUDY OF SUXAMETHONIUM INDUCED MUSCLE FASCICULATIONS, POST-OPERATIVE MYALGIA AND HYPERKALEMIA WITH THE PRECURARIZATION AND SELF TAMING OF SUXAMETHONIUM" which is being submitted as a thesis for M.D.(Anaesthesiology) by Dr. Daya Shankar, has been carried out by the candidate himself in the Department of Anaesthesiology, M.L.B. Medical College, Jhansi (U.P.).

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This thesis fulfils the basic ordinance governing the submission of thesis for M.D., laid down by Bundelkhand University.

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INTRODUCTION

INTRODUCTION

Suxamethonium, a dicholine ester of succinic acid, is the short acting depolarizing muscle relaxant. It is extensively employed in modern anaesthetic practice owing to its property of providing excellent muscular relaxation of rapid onset. Usual I.V. (1-2 mg/kg) doses of suxamethonium produce excellent endotracheal intubation conditions within 10-30 sec. The associated muscle relaxation persists upto 5 mts, thus making it relaxant of choice during numerous diagnostic and surgical procedures of short duration such as Endoscopies, bronchoscopy, orthopaedic manipulations, anal dilatation and modified electro-convulsive therapy. It can also be of immense help in the form of intermittent doses even during major surgical procedures when non-depolarizing muscle relaxants are not desirable.

This drug is rapidly hydrolysed by the pseudo-cholinesterase, an enzyme of plasma, as soon as it enters the circulation. Thus only a fraction of administered drug reaches the neuromuscular junction where it acts as agonist over the prejunctional and junctional receptors. Response of junctional receptors produces weak but persistant depolarization of motor end plate, making it

unresponsive to the acetylcholine. Thus depolarization type of neuro-muscular block is established resulting into muscular relaxation.

Inspite of enjoying reputation of an ideal muscle relaxant drug has certain adverse effect associated with its use. Its agonistic action may lead to the development of Bradycardia and bronchospasm, besides these production of neuro-muscular block itself is preceded by fasciculation or muscle twilches alongwith increase in intra-gastric and intra-ocular pressure. Subsequently hyperkalemia, although mild and transient in healthier patients, occurs during induction period, and may be fatal in certain cases. The above mentioned problems are to be faced immediately after the suxamethonium administration but post-operative period is also important since unpleasant myalgias and myoglobinuria may occur even some days after surgery.

In addition to these potential problems suxamethonium induced prolonged apnoea and malignant hyperpyrexia may create a grave situation in susceptible patients. The administration of larger doses such as during multiple intermittent doses or I.V. infusion may lead to the development of Phase II block.

The muscle fasciculations almost always precede the development of neuro-muscular block and perhaps are the result of pre-junctional receptor stimulation by the

suxamethonium. They are usually seen as fine tremors over face, finger and toes but coarse and vigorous twitching may occur with occasional unco-ordinated movements of trunk and limbs.

Severity of visible fasciculation is altered by induction technique, mode of suxamethonium administration and various preventing measures including precurarization and self taming.

Post-operative suxa-pains are really troublesome and occur in majority of patients. They may be generalized or localized with the varying intensity from mild aches to severe incapacitating muscle pain and stiffness. The onset is usually within 24 to 48 hours and usually persist upto three and rarely upto 5-6 days.

Incidence and severity of myalgias are much higher in adult and middle aged patient. Females, except during pregnancy are more susceptible while children, elder patients and muscularly fit persons have been found to be less prone. Besides patient factors anaesthetic technique, position of patient, nature and duration of surgery also alter the development of such pains.

Etiology of such pains is still unknown but muscle damage due to suxamethonium is the most probable cause. Numerous measures were and are being adopted for prevention of these pains because it seems incongrous to induce pain

by the discipline of anaesthesiology which is established to conquer the pain. Moreover, the discomfort of suxamethonium pains may even exceed that of actual operative procedure and occasionally make the patient bed-ridden and delay their stay period in the hospital.

Self taming and precurarization are among the most useful preventive measures against the occurrance of the adverse effects of the suxamethonium.

Self taming of suxa-fasciculations has been introduced in 1977 when Baraka successfully attenuated them with the help of small pre-treatment dose of suxamethonium itself. Subsequently, similar attenuation of suxa-fasciculations has been reported by Verma (1979), Wilson, Dundee (1980) and Gillani et al (1980). However, self taming dose itself may induce mild fasciculations in some cases. Hyperkalemic response to suxamethonium has also been shown to be inhibited after the self taming (Thatte et al, 1980; Magee, Gallaghar, 1984). However, Wilson, Dundee (1980) have failed to suppress the incidence of suxa-pains with the help of this pre-treatment.

Precurarization is perhaps the most widely used preventive measure in which small pre-treatment dose of a non-depolarizing muscle relaxant is given 2-3 mts. prior to the administration of suxamethonium. Gallamine (40 mg.) was the first drug to be used for such pre-treatment (C. Davidson, 1954). Subsequently, smaller doses of

Gallamine from 5 mg (White, 1962) to 20 mg (Bennetts, Khalil, 1981) have been recommended for this purpose.

Morris Dunn (1957), Mayrhofer (1959) have successfully used tubocurarine as precurarization drug since then almost every available non-depolarizer has been evaluated for this efficacy (Weintraub, 1969; Miller, Way, 1971; Cullen, D.J., 1971; Brodsky et al, 1979; Bennetts, Khalil, 1981; Ferres et al, 1983; Masey et al, 1983 and Sullivan, 1988).

Among the Gallamine, d-tubocurarine and Pancuronium the Gallamine has been described as best effective by Cullen (1971) but Casey et al (1981) have found the Pancuronium to be a better choice and Erkole et al (1983) have considered the d-tubocurarine to be most effective. Contradictory to the aforesaid reports, Ferres et al (1983) have selected the Vecuronium to be drug of choice. Similarly, many other investigators have reported variable but definite efficacy of various non-depolarizers against the adverse effects of suxamethonium. However, associated antagonism of suxa-paralysis leading to poor intubating condition has remain a potential problem when the method of precurarization is employed.

REVIEW OF LITERATURE

REVIEW OF LITERATURE

Suxamethonium Chloride :

The drug was first prepared by Reid Hunt and Taveau in 1906. But they failed to recognise its muscle paralysing property because they were using the drug on the previously curarised animal. This valuable property of drug remained obscured for about 40 yrs when Bovet et al (1949) in Italy and Phillips (1949) in U.S.A. described the neuro-muscular blocking action of the drug. Castillo (1950) and E. de Beer (1950) also observed muscular paralysis of rapid onset and short duration. Soon the drug was accepted for clinical anaesthesia and was popularized by Von Dardel O, and Thesleff, S. (1951) in Stockholm, Buck et al (1951) and Mayrhoffer, Hassfurther (1951) in Austria, Bourne et al (1952) in Great Britain and Folder (1952) in U.S.A.

Chemically, suxamethonium is a synehetic Bisquaternary compound and a dicholine ester of succinic acid, which consists of two acetylcholine molecules, joined back to back.

It is a white crystalline substance which is relatively unstable and deteriorate rapidly in warm atmosphere and alkaline pH. Chloride salt of suxamethonium

is relatively stable but to be stored at 4°C as hydrolysis may occur at room temperature.

The intravenous bolus of suxamethonium (1-2 mg/kg) is the most prefered route with the average intubation dose of 25 - 100 mg. Onset of paralysis occurs within 10 - 30 seconds and duration of action varies from 1 to 5 mts.

Drug is not effective orally but can be given intra-muscularly but with reduced efficacy. I/V infusion can also be used to obtain sustained action with the rate of 16 mg/kg/mt.

The extremely brief duration of action is because of very rapid hydrosis of suxamethonium by an enzyme, plasma cholinesterase which is a glycoprotein synthesized in liver and present in plasma. This enzyme is among the most potent enzyme of body and has an enormous capacity to hydrolyze the drug into succinyl monocholine and choline. Foldes and Norton (1954) found that this rapid hydrolysis occurs within second after intravenous administration of drug and infact only about 5% of drug reaches to action site.

Succinylmonocholine, thus produced, is also but a weak neuromuscular blocking agent and slowly hydrolysed into succinic acid and choline by a specific enzyme (Greenway and Quostel, 1953).

Since there is lack of plasma cholinesterase at motor end plate the action of drug is terminated by its

diffusion away from neuro-muscular junction to the extra-cellular fluid and by redistribution to the liver, spleen kidney, muscle and plasma. Only about 2% of drug is excreted through kidneys unchanged.

Alkalin hydrolysis, a non-enzymatic metabolism, also occurs but it is extremely slow and only 5% of drug/hr. is metabolised by this route (Kalow, 1959).

Suxamethonium acts as agonist at neuro-muscular junction over the post-junctional receptors, specialized sodium channels which consists of lipoprotein molecules embeded in cell membrane of motor end plate. Each receptor contains two alpha, one beta, one gamma and one delta sub-units. When suxamethonium molecules occupy both of alpha sub-units other three rotate to form a new configuration. As a result channel become to open to allow Na^{+}/Ca^{++} influx and K+ efflux according to ionic concentration gradient. This ionic rearrangement causes prolonged depolarization of weak intensity at the motor end plate to initiate propagatory impulse all over the muscle fibres.

Since suxamethonium stays at neuro-muscular junction longer than acetylcholine, thus the motor end plate becomes refractory to further stimuli. Receptors remain open and depolarization type of neuro-muscular block occurs leading to complete muscular relaxation. Such type of block is commonly known as Phase I block, characterized by -

1. Occurrance of fasciculations,
2. Sustained single or tetanic twitch height,
3. Absence of post-tetanic fasciculation,
4. T_4 / T_1 Ratio : 7.7
5. Potentiation of block by anti-cholinesterases, e.g. Neostigmine.

Fasciculations :

Fasciculations are observed visually, soon after suxamethonium administrations, as transient and inco-ordinated muscular twitches usually of face, limbs and abdominal muscles. Intensity remains variable and ranges from minimal surface twitching of eyelids or fingers to mild or moderate generalised coarse twitches often associated with limb movements. Occasional occurance of vigorous incoordinated shaking of trunk and extremities is also not uncommon, however intense they may be, but subside as soon as muscular relaxation supervenes (Durant, Katz, 1982).

Visible degree of fasciculations may well be a characteristic of an individual muscle but is also modified by thickness of subcutaneous tissue (Kitamura et al, 1981) and by the rate of presentation of the drug at neuro-muscular junction. Rapid circulation time of patient or rapid injection of suxamethonium have been associated with vigorous fasciculation (Newnam, Loudon, 1966) while slow injection reduces the severity of fasciculation (Domaoal et al, 1975). Obviously, dose of suxamethonium is also

important as water and Mapleson (1971) have observed severe fasciculation but of shorter duration after a bolus of longer dose. Thiopentone induction is also known to suppress the fasciculation (Burtles, Tunstall, 1961 and Craig, 1964).

Etiology of fasciculations is still in controversy. Initially Davidson and Richardson (1952) postulated suxamethonium induced motor unit stimulation to be a causative factor. Later Davidson (1956) observed that stimulation of even a single motor and plate activate whole motor unit through the antidromatic axon reflex.

Paton (1959) has made another hypothesis suggesting that suxamethonium stimulate intrafusal fibres resulting into sustained contracture of muscle spindles which in turn generate a series of motor unit discharge leading to development of fasciculations. Kato et al (1965) also supported this mechanism.

At present concept of pre-junctional receptor response to suxamethonium is most acceptable. A number of quanta of acetylcholine are supposed to be released due to this response and act over motor end place to produce the fasciculation (Kitamura, Yoshia and Nagishi, 1981).

Foldes et al have observed the feeling of fasciculations in conscious volunteers even in absence of any visual sign and visual monitoring has been found

inadequate in assessing the degree of depolarization of motor end plate by Burtles, Tunstall (1961). Electro-myographic recording has been considered to be a better alternate (Fozard, Manferd, Harris, 1971).

Recently Jansen and Hensen (1979) have succeeded in development of an electronic device to monitor the fasciculations by recording the variation in arm circumference. Fasciculations quantified with such an electronic counter have shown definite correlation with the numbers of visible counts.

Myalgia :

Post-operative myalgias have remained frequent and unpleasant effect of suxamethonium. They were recognised soon after introduction of the drug in clinical practice. Dardel, Thesleff (1952) draw attention and Bourne, Collies and Somers (1952) suggested suxamethonium as a possible cause for such pains. Sanger et al (1953) related them to the use of all depolarizing muscle relaxant.

Nature of pain resembles with that occur after violent and vigorous exercise of unaccustomed muscles (Leatherdale, Mayhew and H. Williams, 1959; and White, 1962). Patients may describe the pains and stiffness like suffering from flu or they feel that they have been mauled about (Burtles, Tunstall, 1961).

Common sites are the neck, the shoulders, anterior chest wall, lower chest cage and the upper abdomen usually in that order (Burtles, Tunstall, 1961), followed by the jaw, limb (Bryton, Ormston, 1962) and upper and lower back (Parbrook, Pierce, 1960). Post-operative sore throat is also considered to be a part of pain syndrome as it is a result of similar etiology (Levon, M., Capon et al, 1981).

Intensity of pain vary from mild aches to severe incapacitative pain at a single or multiple sites (Burtles, Tunstall, 1961). They are precipitated or exaggerated when muscle is used during movement and more commonly remain localized at one or two sites (White, 1962). Localized severe pain may mimic Pleurisy (Curie, 1953) or meningitis (Price, 1954).

Onset of pain has been found to remain within 24 hrs (Parbrook, 1960) to 48 hrs (Haldin Palmer, 1961), but occasional patients may suffer within 3 hrs (Craig, 1964) or after 96 hrs (Burtles et al, 1961). Pains usually persists for 3 days (White, 1962 and Parbrook, 1960) but may remain for upto 6 days (Burtles, 1961). Inspite of variable onset, it is almost certain that incidence is higher after early ambulation as suggested by C. Davidson (1954). Burtles, Tunstall (1961) have found Myalgia in 69% patients who became ambulatory on Ist day while it was less on subsequent days of ambulation e.g. 53% on 2nd day and 47% on 3rd day.

Reported incidence of myalgia is not uniform and ranges from 1.2% (Crawford, 1971) to 89% (Mayrhofer, 1959). Other reports have suggested as under : 25% (Hegar, 1956), 40% (Prince White, 1957), 75% (Richards Burtles, 1961), 85% (Foster, 1960), 41% (Ferres et al, 1983) and 52% (Magee and Robinson, 1987).

These wide variations are thought to be the result of influence of several factors which include patients age, sex, muscular fitness, nature and duration of surgery, position during operation, type of premedication, induction and mode of administration of suxamethonium. The manner of questioning for history of pain and subsequent response from the patient may also alter the results.

Children and patients over 50 years are less prone to have myalgia (Bush & Roth, 1961). Burtles, Tunstall (1961) have observed less myalgia (2.6%) in patients of more than 60 years age. According to Thind & Bryson (1983) children have more elastic collagen fibres so are less prone to muscle spindle damage.

Leatherdale et al (1960) have observed higher incidence in females in comparison to males, in the ratio of 2 : 1 while Burtles et al (1961) reported a frequency of 59% in females and 49% in males. Riding (1975) and Magee, Robinson (1987) also have observed higher incidence in females. Most investigators are agreed but Foster (1960) has found no difference in incidence on the basis of sex.

Although females tend to be highly susceptible to develop myalgia, pregnancy has a protective role against this tendency (Crawford, 1971) and it may be kept equivalent to precurarization with 5 mg tubocurarine or 40 mg Gallamine (Dutta et al, 1977).

Crawford (1971) concluded that pregnant women are 50% less susceptible than their non-pregnant counterparts, perhaps because of high progesterone concentration in the tissue prevents muscle damage due to suxamethonium. Almost similar observations were made by Dutta, Crocker and Alper (1977) when they detected less cases of severe fasciculation (28%) and myalgia (20%) in pregnant women when compared to fasciculation (68%) and myalgia (42%) occuring in non-pregnant. They postulated the rapid dilution of suxamethonium because of higher plasma volumes to be reason of such result.

Efficacy of pregnancy was confirmed by Thind and Bryson (1983) who have described fasciculations (88.7%) and myalgia (7.5%) in pregnant to be significantly lower than non-pregnant who had fasciculations 97.5% and myalgia 30%. This time oestrogen was postulated to be protective agent against the suxamethonium induced muscle damage.

Davidson (1954) has described higher incidence in out patients (66%) than in-patients (14%), Morris & Dunn (1957) have found this ratio to be 72 : 35. Leatherdale et al (1959), Burtles, Tunstall (1961) and D.C. White (1962)

also have supported the view that out-patients are more susceptible to have myalgia because they tend to remain mobile while in-patients usually prefer recumbency during post-operative period. In contrast, Price et al (1960) and Bennette, Khalil (1981) observed no difference between two groups.

Morris Dunn (1957) and Leatherdale (1959) have reported definite relationship between incidence of myalgia and the physical fitness and muscle power but Haldin Palmer (1961) showed increased tendency of myalgia in patients with less developed musculature. Newnam & Loudon (1966) have emphasized that muscular fitness is an important factor and myalgia is less likely in patients with good muscular fitness.

Magee and Robinson (1987) have established the role of muscular fitness when they were able to reduce incidence of myalgia from 52% to 12% by pretreating patients with certain stretch exercises about 1 hr. before surgery.

Nature of operation also influences the myalgia by determining the length of surgery and the position of patient. Pain of surgery may mask the suxa-pains and it may be super imposed over same site. Patients after minor surgery detect suxa-pains easily because it may be more severe than that of operation (Craig, 1964).

Unaccustomed postures and positions produce their own pains e.g. higher incidence of low backache after lithotomy position are known.

Theories of Pains :

The exact mechanism of suxamethonium pain remains mysterious. Initially they have been considered to be related to occurrance of visible fasciculations (Davidson, 1954), and incidence of severe pains were attributed to the vigorous fasciculations (Bennike, Neilsen, 1964).

Morris, Dunn (1957), Leatherdale et al (1959) and Burtles, Tunstall (1961) contradicted any such correlationship and even vigorous fasciculation of short duration have been observed to be associated with reduction in incidence and severity of suxamethonium pains (Haldin and Palmer, 1961).

Subsequently most of the investigators failed to establish the correlationship between occurrance of suxamethonium fasciculations and suxa-pains (White, 1962; Collier, 1975; Magee et al, 1977; Bennetts and Khalil, 1981; Ferres et al, 1983).

Waters Mapleson (1971) have postulated that finer fasciculation may induce more muscle damage due to increase in the number of sites of shearing force between muscle fibres.

Numerous mechanisms have been postulated to explain the occurrance of suxamethonium pains.

1. Lactic acid production as a result of vigorous fasciculations (Von Konig, 1956).

2. Accumulation of succinyl-monocholine (Paton, 1959).

3. Potassium release from the muscles (Mayrhofer, 1959).

4. Release of intrinsic algogenic substances into the extra-cellular fluid has been postulated by Keele and Neil (1974). Some of these substances are thought to be A.M.P., A.D.P., A.T.P., Histamine and a cationic protein from the leucocytes.

5. Prostaglandin synthesis and release may be an important factor (Naquib, 1987).

6. Muscular tissue damage due to unsynchronized contractions is the most acceptable factor, although mechanism and site of muscle damage remains controversial.

Water & Mapleson (1971) have hypothesized that suxamethonium reaches different myofibrils at different times as vascular supply of adjacent fibres may not be equally distributed. As uncoordinated fasciculations occur as contractions of some fibres occurs earlier than that of adjacent fibres leading to the development of shearing force between the contracting and awaiting fibres. This shearing force may be the chief cause of muscle fibres damage and subsequent creatinine phosphokinase release and after-pains.

Collier (1975) has suggested muscle spindles damage to be the primarily responsible to cause suxamethonium pains. This site seems to be reasonable because most commonly pains are noted in the muscles having high spindle counts e.g. muscles of back of neck, lower thoracic cage.

Irreversible changes in muscle spindles following suxamethonium administration have been found and are attributed to the mechanical damage in the spindle structure (Rack and Westbury, 1966). This breakage may itself result from ability of suxamethonium to produce sustained contractures of the spindle fibres due to stimulation of intrafusal fibres (Bessov et al, 1968).

Meadows (1971) has observed tetany in spindles to occur after the high frequency of action potential generation at motor end plate by the suxamethonium. Collier (1975) has more appropriately suggested critical threshold frequency of motor unit discharge to remain 50 Hz after which spindles contracture and damage is most likely to occur.

Muscle spindle damage as a cause of suxamethonium pain also explains the occurrance of post-operative sore throat, as Laryngeal muscles contain high spindle density.

Incidence of suxamethonium pain are most common during late post-operative period because spindle damage is associated with the loss of fine control during movement in early ambulation period. Thus, overstretching of muscle

similar to that after vigorous exercise, may occur which are subsequently recognised as myalgia.

Hyperkalemia :

Klupp, Kobinger and Krupp (1954), in animal experiments, has demonstrated evidence of dose dependent rise in plasma potassium concentration after suxamethonium administration. Since then suxamethonium is well known to possess the property to induce a mild and transient rise in the plasma potassium concentration which ranges from 0.09 m mol/L (List, 1967) to 0.66 m mol/L (Kumar et al, 1987), more than pre-induction value. Peak levels are reached within 7 minutes (Weintraub, Heisterkamp and Cooperman, 1969) and usually persist upto 10 minutes (Bali, Dundee, 1974; Thatte et al, 1981) or even upto 15 minutes (Mazze et al, 1969; Konchigeri et al, 1976; Jassal et al, 1976).

Paton (1956), List (1967), Striker, Morrow (1968), Anand et al (1972), Bali, Dundee (1974), Thatte et al (1981) & Magee et al (1984) also have concluded that this hyperkalemic response occurs after the suxamethonium administration.

The exact mechanism of such hyperkalemic response remains in mystery, however, it is certain that muscle tissue acts as source of potassium (Paton, 1954; Bali, Dundee, 1974). This release has been attributed to gross muscular fasciculations (Klupp et al, 1954; Bali, Dundee, 1975). Indirect

evidence also has suggested that muscle damage due to fasciculation may induce leak of intra-cellular muscle contents such as creatinine phosphokinase and myoglobin (Tommisto, Airaksinin (1967). Roth and Wuthrich (1967) have postulated that potassium is released from the muscle cells due to cell membrane injury during the development of shearing force between the muscles cells at the time of fasciculations.

Mayrhofer (1959) and Hegab et al (1976) have reviewed the hypothesis regarding fasciculation induced muscle damage but no microscopic evidences were concluded to prove such a damage. Jassal et al (1974) also failed to establish any correlationship between suxamethonium induced fasciculations and hyperkalemia. Moreover, John and Tobay (1976) have reported cases of massive hyperkalemic response even in absence of visible fasciculations. Wintraub et al (1969) have observed equivalent hyperkalemia with the suxamethonium and decamethonium while later resulted into minimal fasciculations.

It has been postulated that "depolarization of any excitable membrane generally leads to potassium release from the cell concerned" (Paton, 1959). Paton (1959), Stevenson (1960) and Gronert (1975) have demonstrated definite role of suxamethonium induced depolarization to release potassium from muscular tissues. Magnitude of

Potassium release has been supposed to be very large as each molecule of suxamethonium may displace about 1500 K^+ while only 5-10 K^+ can be displaced by a molecule of acetylcholine.

Collier (1978) has suggested that major fraction of potassium efflux occurs during depolarization which leads to subsequent electro-mechanical coupling. As a result additional potassium release may be contributed at the time of fasciculations. The released potassium enters the circulation and is soon taken up by the liver. Later, it is redistributed to the muscular tissue where re-uptake is processed (Fenn, 1940).

List (1967) has observed, after the thiopentone induction, the significant fall in the mean plasma potassium concentration from 4.20 m mol/L to 3.81 m mol/L (mean fall 0.39 m mol/L), but the subsequent administration of the suxamethonium raised the mean potassium concentration to become 3.90 m mol/L to produce the mean rise of 0.09 m mol/L. Coincidently, the mean rise, after the suxamethonium, was observed to be 0.27 m mol/L when the induction was performed with the mixture of O_2+ N_2O + Halothane.

Mazze et al (1969) have shown mean plasma potassium concentration to rise from pre-induction value of 3.8 m mol/L to become 4.2 m mol/L (at 2, 3 and 4 minutes), 4.1 (at 5 minutes) and 4.0 m mol/L (at 7½, 10 and 15 minutes) with the maximum rise of 0.6 m mol/L to occur.

Millar, Way, Hamilton, Layzer (1972) also have shown gradual and sustained change in potassium level from 3.7 m mol/L to 3.6 (at 2 minutes), 4.0 (at 5 minutes) and 3.8 m mol/L at 7 and 10 minutes, with the maximum rise of 0.18 m mol/L at 5 minutes.

Konchigeri et al (1976) have reported the mean plasma potassium concentration to be 3.56 m mol/L (pre-induction), 3.99 (at 2 minutes), 3.81 (at 3 minutes), 3.80 (at 5 minutes), 3.66 (at 15 minutes) and 3.64 (at 15 minutes) after the administration of suxamethonium.

Jassal et al (1976) have measured the mean plasma potassium concentration to rise from 4.40 m mol/L (pre-induction) to 4.5 at the time of fasciculations. The potassium level again raised to 4.81 m mol/L at 5 minutes and 4.51 at 15 minutes.

Thatte et al (1981) have shown a rise of 0.1 m mol/L between 3 - 5 minutes and of 0.2 m mol/L at the interval of 10 minutes.

Naquib et al (1987) have shown this rise to be of 0.1 m mol/l at 3 minutes but the potassium level returned to pre-induction value of 3.9 m mol/L.

Kumar et al (1987) also have observed a rise of 0.66 m mol/L when the mean potassium levels was raised from 3.88 m mol/L to 4.54 m mol/L at the interval of 5 minutes.

The usual mild rise in potassium concentration is of little clinical significance in healthy patients but the suxamethonium may induce massive hyperkalemia in certain susceptible patients suffering from burns, tetanus, massive trauma, neurological disorders including upper and lower neurone disease, denervation injuries and chronic renal failure. In such cases plasma potassium concentration have been reported to increase even above the level of 10 m mol/L which is sufficient to cause fatal ventricular arrythmia (Gronert, Theye, 1978 and Imatsuki et al, 1980).

In fact, numerous incidences of unexplained cardiac arrest have remained associated with the induction of anaesthesia. Forrest (1959) suspected suxamethonium to be a probable cause of these cardiac arrest. More appropriately Finer and Nylen (1961) attributed them to the hyperkalemic response to suxamethonium. Davis et al (1961) and Allan et al (1961) also reported occurrance of fatal cardiac arrythmias in patients showing massive hyperkalemic response to suxamethonium.

According to Gronert (1975), only 1% loss of total potassium content of muscular mass may sufficiently achieve the plasma potassium concentration to rise above 10 m mol/L. Total potassium in muscle can be calculated in an average weight (70 kg.) patient containing 40% muscle. Each 100 gms of muscle has 5 mEq of potassium (50 m mol/kg.) thus, total potassium content would be 1400 m mols.

Burn :

Induction of anaesthesia in severely burnt patients has been reported to remain very critical period as multiple incidences of fetal cardiac arrythmia has occurred (Allen, Cullen, Gillies, 1961; Bush, 1964; Belin 1966; and Tolmie et al, 1967). Several factors such as hypovolumia (Forrest, 1959), extreme bradycardia (Fleming, 1966) and pseudo-cholinesterase depletion were related to such incidences but most probable cause seems to be the suxamethonium induced hyperkalemia.

Tolmie, Joycee and Mitchell (1967) reported accurence of ventricular fibrillations in a burnt patient soon after receiving suxamethonium. E.C.G. changes were suggestive of hyperkalemia and plasma potassium concentration was measured to be very high (7 8 m mol/L). Similarly, Schaner et al (1969) observed plasma potassium concentration to remain 7 6 m mol/L in a burned patient.

The increased susceptibility in these patients may be attributed to the muscle mass damage (Cooperman, 1970) and disuse atrophy (Kalow, 1973) both factors are known to induce the super-sensitivity of muscle to release excessive potassium in response of suxamethonium (Gronert, 1975).

This super-sensitivity begins to appear within 5-15 post-burn days and may persist for 2-3 months (Gronert, 1975). Earlier also, it has been reported that

burn patients are most prone to develop cardiac arrest during induction of anaesthesia between 21st and 51st post-burn days (Caughey, 1962).

Tetanus :

Roth and Wuthrich (1969) have reported this massive response in patients of tetanus, massive trauma and uraemia. In the presented series of such patients, some of them showed E.C.G. changes suggestive of hyperkalemia. A tetanus case had definite rise in plasma potassium concentration from 3.8 m mol/L to 9.4 m mol/L within 2 minutes of receiving suxamethonium. Similar higher plasma potassium concentration (7.1 m mol/L) was also measured in a patient of massive trauma at the time of suxamethonium induced cardiac arrest.

Muscular degeneration and necrosis occurs in tetanus patients from second week onwards (Stirnemann, 1967; Brody et al, 1967 and Eyrich, 1967). These patients tend to develop super-sensitivity of the muscles in response to acetylcholine or suxamethonium leading to hyper-reflexia or hyperkalemia respectively. The risk of massive hyperkalemia may persist for indefinite period or at least upto 6 months.

Trauma :

Roth et al (1969) established higher susceptibility to develop suxamethonium induced massive hyperkalemia in

patients of massive muscular injuries. In such a patient, plasma potassium concentrations were measured to be 7.1 m mol at time of suxamethonium induced cardiac arrest.

Mazze, et al (1969) also have reported an increase in potassium concentration from 3.7 m mol/L to 6.8 m mol/L with maximum rise of 9.5 m mol/L in such patients.

Later, Rama Rao et al (1976) reported occurrance of cardiac arrythmia and relatively large hyperkalemic response with the rise of 7 1 m mol/L at about 7 minutes after receiving suxamethonium.

These patients have been supposed to develop super-sensitivity (Cooperman, 1970) about 3 weeks after sustaining the injury and it persists till complete healing of wounds (Mazze et al, 1969). However, risk is minimized during acute phase of injury as Charles Kopriva et al (1972) have successfully administered suxamethonium in such patient only to found a slight rise in plasma potassium concentration (+ 0.4 m mol/L), when patients were anaesthetized within 3 hours of sustaining the injuries.

Neuro-muscular disorders :

A wide variety of neurological and muscular disorders are known in which patients become highly susceptible to the suxamethonium hyperkalemia. Such disorders include -

1. Lower motor neurone lesions - Denervated injuries, Nerve degenerations, Neuropathies; 2. Upper motor neurone lesions - Spinal cord injuries, Encephalitis, Cerebro-vascular accidents, Head injuries; 3. Prolonged immobilization - After tenotomy, Internal or external fixations; 4. Myopathies, muscular trauma and degeneration.

Stone et al (1970) observed a marked rise in plasma potassium concentration from 4.3 m mol/L to 5.6 m mol/L in a paraplegic patient, at the 23rd day after sustaining spinal cord injury. Raymond, Tobey (1970) proved the susceptibility of paraplegia patients when such patients showed plasma concentrations to be 7.3 and 11.0 m mol/L after the administration of 30 and 80 mg suxamethonium infusion. Peak level of 13.6 m mol/L was measured but patient had a cardiac arrest. Coincidentally, potassium concentration in blood drained from lower extremities were much higher.

Cooperman (1970) observed an immediate, persistant and marked rise in potassium concentration from 3.8 m mol/L to 8.95 (at 3 minutes), 9.05 (at 5.5 minutes) and 6.5 (at 11.5 minutes) alongwith the well correlated E.C.G. changes after suxamethonium in the patients suffering from upper motor neurone lesion.

Similar response has been reported in a hemiplegic patient (Stone et al, 1970) in which potassium concentrations was raised from 4.5 to 11.6 m mol/L within minutes of receiving suxamethonium.

Cowgill, Lucille (1974) observed mean plasma potassium concentrations to show massive and persistant increase from 3.59 to 10.52 (at 90 seconds), 7.29 (at 5 minutes) and 6.13 m mol/L (at 30 minutes) in a encephalitic patient. Patients of closed head injuries also have shown exaggerated hyperkalemic response to suxamethonium (Stevenson and Birch, 1971; Frankvilli and Drummod (1987).

Patients of various muscular diseases such as pseudo-hypertrophic muscular dystrophy (Genever, 1971), myosarcoma (Cairoli, 1982) and rhabdomyosarcoma (Laura et al, 1989) are also reported to be susceptible to suxa-hyperkalemia.

Exact mechanism of increase in susceptibility in neurological patients is uncertain. Muscular tissue of such patients are supposed to develop the neurotropic changes similar to those which use to occur after denervation. In the case of upper motor neurone lesion, the loss of higher centres influence leads to occurrence of trophic changes at anterior horn cells in spinal cord to make the lower motor neurone inactive (Gronert, 1975). Loss of neuronal activity induces impairment of membrane ion permeability (Thesleff, 1963) and active ion transport (Dockry, 1966) in the muscle cell membrane leading to excessive leak of potassium during chemical excitation. Kending et al (1972) and Kruger (1973) have postulated that entire muscle surface become responsive to suxamethonium.

Gronert (1975) have suggested that extrajunctional receptors develop the chemo-sensitivity instead of remaining electro-sensitive only. Thus, an equivalent magnitude of depolarization may result into excessive potassium efflux from larger muscular super-sensitive area.

Similar super-sensitivity is also known to occur during prolonged disuse of innervated muscle. Magnitude of this response remains mild to moderate because even minimal neuronal activity preserves some muscle tone and prevents the trophic changes in muscles to occur. Moreover, these changes tend to return towards normal when muscle is re-used or external stimulation to the nerve is applied (Gronert, 1975).

Uremia :

Roth et al (1969) have reported an uremic patient who showed significant rise in potassium concentration from 6.5 to 8.9 m mol/L after suxamethonium administration. Similarly, Powell (1970) measured an increase in potassium concentration from 4.1 to 6.9 m mol/L.

However, Millar and Way (1972) have observed no significant difference among the uraemic and non-uraemic patients regarding this response as rise in potassium concentration remained + 0.7 and + 0.6 m mol/L respectively. Similarly, Koide and Ward (1972) have reported only a slight rise (+0.52 m mol/L) of plasma potassium concentration in uraemic patients.

Infections :

Kohlschutter (1976) reported this response in the patients of severe intraperitoneal infection, in which potassium concentration were increased (+ 2.5 to +3.1 m mol/L) after suxamethonium.

Khan and Khan (1982) have attributed the magnitude of hyperkalemic response to the severity and duration of infections and maximum hyperkalemia occurs between 8 - 21 days after severe infection. Rise in serum potassium levels were found to vary within range of 0.2 - 2.3 m mol/L depending upon severity of infection.

Numerous measures have been applied to prevent suxamethonium induced fasciculations, myalgia and hyperkalemia.

1. Succinyl bromide in place of succinylcholine has been said to induce less myalgia (Rudell et al, 1959) but no significant difference was observed by Leatherdale et al (1959).

2. Suxa-ethonium substitution for suxamethonium has been suggested by Enderby (1959) but Parbrook and Pierce (1960) contradicted this view.

3. Change in route of suxamethonium administration from intravenous to intramuscular was not found to be very effective as incidences of myalgia were 28.6 and 26.6% respectively (Cooke et al, 1963).

4. Suxamethonium as slow I.V. infusion (0.2%) has been found to reduce incidence of myalgia from 40% to 14% (Lomoreax et al, 1960), because only initial exposure to the drug induces the muscle damage and relatively less myalgia (Water & Mapleson, 1971), however White (1962) has observed reduction in fasciculations with this procedure but incidence of myalgia remained unaffected.

5. Slow I.V. administration as a single dose has remain ineffective (Morris Dunn, 1957). However, rapid injection of larger dose of suxamethonium has reduced the suxa-pains but associated with the more severe fasciculations (Haldin Palmer, 1961).

6. Self Taming by using small dose of suxamethonium (10 mg.) prior to the full paralysing dose (1 to 1.5 mg/kg) has been found effective in prevention of fasciculations (Baraka, 1977) but inhibition of myalgia remains controversial.

7. Hexafluramium bromide (Foldes et al, 1961), chlor-promazine (Morris & Dunn, 1957), Atropine sulphate with neostigmine (Foster, 1960) also have been used but remains unsatisfactory.

8. Xylocaine has effectively reduced the incidence of myalgia. It can be used as Single I/V bolus of 6 mg/kg lignocaine (Usubiago, 1967) or as 1% I.V. infusion in the dose of 3-4 mg/kg (Haldia, 1975) or as topical spray of 10% xylocaine with total dose of 90 - 110 mg (Fassoulaki et al, 1981).

9. Vitamin C administration as 500 mg twice orally one day before has remain effective in prevention of fasciculations and pains but hyperkalemic response remains unaltered (Gupta, Savant, 1971 and Kumar et al, 1988).

10. Dantrolene has significantly reduced all the adverse effects of suxamethonium in the dose of 100 - 150 mg oral 2 hours before the induction of anaesthesia (Collier, 1979).

11. Magnisium sulphate has been shown to abolish suxa-fasciculations and rise in plasma potassium but not the suxa-pains (Aldrete, 1970; Devore, 1980 and Chestnutt, Dundee, 1985).

12. Calcium gluconate as 10% solution in dose of 10 ml I.V. slow just before the induction have been shown to effectively reduce myalgia from 45% to 5% alongwith significant inhibition of hyperkalemic response (Shrivastava et al, 1983).

13. Diazepam (10 mg/I.V.) pre-treatment about 5 minutes prior to suxamethonium has reduced myalgia (from 60% to 16%), fasciculations and hyperkalemia (Verma, Mathur, 1978; Eisenberg et al, 1979 and Fahury, et al, 1979).

14. Lysine acetyl salicylate (3 mg/kg.) pre-treatment 3 minutes prior to suxamethonium has remain effective to reduce myalgia from 73% to 25% with significant inhibition of suxamethonium hyperkalemia (Naquib et al, 1987).

15. Thiopentone induction - Thiopentone induction has a definite protective role against suxa-pains (Ruddel, 1959) and suxa-hyperkalemia (List, 1967) perhaps because of its capability to reduce the numbers of depolarization sites at motor end plate (W.F. List, 1967).

Burtles and Tunstall (1961) have produced indirect evidence to prove this property of thiopentone. Incidences of myalgia were increased from 24% to 37% when administration of suxamethonium was done before instead of after the injection of thiopentone. Similarly, Henry & Craig (1964) have described myalgia incidence to be increased from 14 to 41% when time interval between administration of thiopentone and suxamethonium is increased from few seconds to 5 mts. The incidence have shown further rise to 56% when thiopentone is replaced by the Halothane as the induction agent.

Effective and consistant fall in plasma potassium concentration also have remain associated with the thiopentone induction (Cloetta et al, 1954; Dobkins & Byles, 1966; Weintraub et al, 1969). Maximum fall in potassium concentrations has been shown to be 0.24 m mol/L (Bali & Dundee, 1974) or 0.23 m mol/L (Konchigeri et al, 1976) less than the pre-induction values. This fall remains significant between 1-4 minutes (Konchigeri et al, 1976).

W.F. List (1967) has reported that thiopentone causes at least 7% fall in plasma potassium concentration. Subsequent hyperkalemic response to suxamethonium is also minimized but not completely prevented by the thiopentone and slight hyperkalemia (+2.3%) is bound to occur.

16. Precurarization with the use of small doses of a non-depolarizing muscle relaxants 1 to 4 minutes prior to suxamethonium has remained perhaps the most widely used measure for prevention of suxamethonium induced adverse effects.

Self Taming :

This term describes the preventive measure in which smaller dose of suxamethonium itself is administered, as the pre-treatment, for the inhibition of after-effects of the subsequent full dose of suxamethonium.

This concept was first thought and evaluated by Burtles and Tunstall (1961) when 5 mg of suxamethonium was considered as a pre-treatment measure and given just prior to the thiopentone, but subsequent observations were not satisfactory. The incidence of myalgia was, rather, significantly raised from 49% in control patients to 75%. In contrast, pre-treatment with 8 mg of Gallamine reduced the incidence to 44%. Thus, it was concluded that even 5 mg

of suxamethonium could result into muscle damage and subsequent muscle pains. Later, a further investigation was carried out to elucidate the protective role of thiopentone and incidence were found to be 37% and 24% when suxamethonium pre-treatment was administered before and after thiopentone respectively.

In fact, the term self taming was introduced by Baraka (1977) when he reviewed the efficacy of pre-treatment with small dose of suxamethonium and found it effective in attenuating the fasciculations. Pre-treatment was administered as 10 mg of suxamethonium after the thiopentone but 1 minute prior to the full paralysing dose of suxamethonium. This measure maintained the excellent relaxation and intubation condition. The pre-treatment with d-tubocurarine 3 mg (3 minutes prior) significantly altered the duration of relaxation to be lessened. Self taming successfully reduced the incidence and severity of fasciculations, as they were observed only in 20% of cases mostly in the form of minimal fascial twitches. However, self taming dose itself induced mild fasciculations in similar number of patients (20%).

Efficacy of self taming in prevention of fasciculation was also proved when R.S. Verma (1979) evaluated the method to inhibit the suxamethonium induced rise in intraocular pressure. Fasciculations were seen in 52% cases with the self taming dose (10 mg) but were reduced to only 4% after

subsequent paralysing dose (100 mg) of suxamethonium. Likewise, self taming dose produced a mean rise in intra-ocular pressure from 11.27 mmHg to 13.8 mmHg, but subsequently 100 mg of suxamethonium remained incapable to induce any further rise. Only one of twenty five patients complained of mild calf muscle pain in post-operative period but such lower incidence of myalgia was attributed to be the effect of Diazepam (10 mg/I.M.) premedication.

Brodsky and Brockutne (1979) have evaluated the efficacy of self taming in prevention of suxamethonium pains but only to conclude this method as an ineffective one. Myalgia occured in 25% of cases whether they were pre-treated with self taming or not. However, associated relaxation was found to be adequate and fasciculations were seen only in 50% patients after second dose (1.5 mg/kg) of suxamethonium. The frequency of fasciculation, immediately after the first (self taming) dose, was found to be 25%. Coincidentally intensity of visible fasciculations was to have no relationship with the incidence and severity of post suxamethonium pains. Vigorous fasciculation were seen in 22% cases but none of them had any myalgia. Similarly, myalgia occurred in patients who were free from fasciculations.

Wilson and Dundee (1980) also have showed self taming to remain effective in prevention of fasciculation, as they were seen in 53% cases after 1st dose (10 mg) but

were abolished after second dose (15 mg). In contrast, occurrence of suxamethonium pain continued to remain high (67%) even after self taming. This frequency did not differ from that (66%) occurred after equivalent dose of suxamethonium (25) as a single bolus. Observations confirmed the view of Water & Mapleson (1971) that frequency and severity of suxamethonium pains might be less with high dose of suxamethonium.

Gilani, Dar and Kangoo (1984) also have proved the efficacy of self taming in successful attenuation of fasciculations. All patients, without self taming, showed visible fasiculations of moderate (80%) to severe (20%) intensity. After suxamethonium pre-treatment, fasciculations of mild (48%) to moderate (12%) intensity were seen in 60% of cases only. Suppression of suxamethonium pains also occurred in significant manner in the pre-treatment group. Overall frequency of myalgia was reduced from 56% to 24%. Mild, moderate and severe pains occurred in 4, 48 and 4% cases respectively when no pre-treatment was administered. After self taming, severe pains were abolished and most patient (16%) had mild and rest (8%) suffered with moderate pains. Incidently no correlationship could be established between severity of visible fasciculations and occurrence of myalgia.

Successful attenuation of suxamethonium fasciculations encouraged Baraka (1978) to postulate the self taming of the

suxamethonium induced hyperkalemia, rise in intraocular and intragastric pressures. Self taming of suxamethonium-hyperkalemia has been shown by Thatte, Mulay and Deshpande (1981) when the mean plasma potassium concentration was significantly reduced to be come less than pre-induction values of 3.9 m mol/L. The mean potassium concentration were measured to be 3.6, 3.7 and 3.7 m mol/L at the respective time interval of 3, 5 and 10 minutes.

Magee and Gallaghar (1984) have succeeded in the prevention of post suxamethonium hyperkalemia with the self taming when mean plasma potassium concentrations showed a tendency to be lowered even less than the pre-induction values. The second dose of suxamethonium was associated with small decrease in plasma potassium concentration (0.22 m mol/L) within 1 minute, followed by a more gradual decrease to reach upto the maximum fall of 0.25 m mol/L at 6 and 7 minutes. In control group, the potassium concentration were significantly raised after suxamethonium, mean plasma potassium concentrations showed a rise of 0.11 m mol/L at 1 minute to reach the peak rise of 0.23 at 3 minutes.

Previously, Baraka (1977) has suggested that neuro-muscular accommodation or desensitation occurs after preliminary small dose of suxamethonium. Subsequent full dose of suxamethonium may then produce blockade without actual electrical excitation of motor end plate and thus

minimize fasciculations and depolarization of muscles as a source of potassium (Magee, Gallaghar, 1984).

However, Sullivan et al (1988) have found the self taming to be ineffective in prevention of the suxa-hyperkalemia.

Precurarization :

Precurarization is among the most effective measures known to prevent suxamethonium induced adverse effects. The term is implied when small dosage of a non-depolarizing muscle relaxants is administered prior to the intubation dose of suxamethonium. The method has been introduced by Davidson (1954) when pre-treatment with small dose (40 mg) of Gallamine successfully reduced the incidence of myalgia from 66% to 40%. Even much lower dose (20 mg) of Gallamine has been proved to be effective in reducing the incidence from 59% to 37% (Foster, 1960).

Richards Burtles and Tunstall (1961) found Gallamine effective even in the dose of 8 mg while pre-treatment with the 5 mg suxamethonium itself increased the myalgia from 49% to 75%, thus suggesting that even smaller dose of suxamethonium might cause muscle damage specially if it is given before thiopentone. D.C. White (1962) confirmed the efficacy of even lower dose of Gallamine (5 mg) when myalgia incidence were decreased from 50% to 29%, with the abolition of severe pains and reduction of fasciculations. However,

incidence of myalgia remained unaffected with the slow injection of suxamethonium.

Morris, Dunn (1957), Mayrhofer (1959) have found d-tubocurarine equally useful for same purpose. Incidence of myalgia was reduced from 83% to 20% with the pre-treatment using d-tubocurarine by Bennike-Neilsen (1964).

Since then pre-treatment with almost all non-depolarizers have been evaluated to have this property. Mechanism of action of such pre-treatment is still unclear. Waud (1968) has postulated that occlusion of a fraction of receptor sites occurs by non-depolarizers leading to development of depolarization of relatively less magnitude. The suppression of the muscle spindle activity may occur by small dose of non-depolarizers making them less susceptible to the suxamethonium induce damage (Collier, 1978).

Apart from the useful efficacy, such small dosage of non-depolarizers have no significant clinical effects except occurrance of occasional diplopia in susceptible cases (Cullen, 1971). Yet this measure received a criticism from time to time, Leatherdale et al (1959) proposed that two theoretically antagonists should not be used simultaneously. Hodge (1957) and Foster (1960) draw attention to the difficulty in respiration associated with such pre-treatment. Moreover, this was categorized to be ineffective in prevention of myalgia by Bryson and Ormston (1962). When they observed insignificant difference in incidence of myalgia with (49.4%) and without (58.5%) pre-treatment.

The development of desensitization block with such pre-treatment may occur (Stovner et al, 1970) because relatively larger dose of suxamethonium is often required to obtain adequate relaxation.

Millar and Way (1971 have monitored the neuro-muscular block in the patients, precurarised either with Gallamine or d-tubocurarine. Degree of block (Twitch magnitude), onset (time to abolish twitch response) and duration (recovery of twitch hight) were found to be significantly similar to those of controls. Except du-tubocurarine reduced the duration of block from 10.9 minutes to 9.4 minutes. Evidence of fade in twitch height and post tetanic fasciculation were absent. Thus any possibility of development of desensitization block were excluded.

Cullen (1971) have compared Gallamine, d-tubocurarine and pancuronium regarding their efficacy and nature of subsequent suxamethonium block. Gallamine (10-20) was found to be most effective in providing adequate relaxation but with a moderate delay in onset (115 sec.) or shortening of recovery period. Adequate relaxation was also obtained with the d-tubocurarine but with significantly delayed onset as abolition of twitches occured at 122 sec. when compared to 63 seconds of controls. Recovery time remained significantly unaltered with all three drugs.

Gallamine has been described to be a better choice than d-tubocurarine (Virtue, 1975) regarding the inhibition of fasciculations. Incidence was lowered from 82% to 12% with Gallamine (30 mg) when given 30 seconds prior to suxamethonium and it became only 2% when Gallamine (30 mg) were used 60 seconds prior to suxamethonium. Pre-treatment with 3 mg (30 seconds or 60 seconds prior) and 6 mg of d-tubocurarine (60 seconds prior) resulted into incidence of fasciculation to be 30% and 18% respectively.

Domabal, Weniger and Wolfson (1975) compared the d-tubocurarine (3 mg) and pancuronium (5 mg) and both efficiently reduced the severe fasciculation and myalgia. d-tubocurarine was superior as it reduced fasciculations from 100% to 5%, which was much lower than incidence of 46% in Pancuronium group. Severe fasciculation and myalgia were abolished from 60% and 20% of the patients respectively. Onset of paralysis, intubation condition and incidence of post intubation coughing were significantly similar with both drugs and comparable with those after suxamethonium alone. However, d-tubocurarine significantly shortened the duration of block from 405.55 seconds to 298.55 seconds.

The pancuronium was found to have more pronounced effect in prevention of fasiculation rather than myalgia (Brodsky, Brockutne and Samuels, 1979). It lowered fasciculation from 95% to 20% and myalgia from 35% to 20%. Moreover, severity of pain remained unchanged. Moderate efficacy of this drug was confirmed by Suma et al (1979) and Wig & Bali (1979).

Hensen and Jansen (1979) observed higher efficacy of pancuronium as it reduced fasciculation count from 277.5 to 37.5, much lower than the fasciculation count of 50.5 in Gallamine group.

Pancuronium was showed to be best effective when compared with Gallamine, d-tubocurarine and Metacurine (Casey Blitt and Carlson, 1981). All drugs produced adequate relaxation, without altering the onset and duration of block.

Agoston et al (1980) reported vecuronium pre-treatment to be quite effective while Eroke et al (1983) studied effects of Alcuronium to be satisfactory.

Bennetts and Khalil (1981) have compared the efficacy of tubocurarine (2.5 mg and 5 mg), Gallamine (10 mg and 20 mg), Pancuronium (0.5 mg and 1 mg) and Fazadinium (7.5 mg and 15 mg). Gallamine effectively reduced the incidence of myalgia on Ist post-operative day from 68% to 33% with the dose of 10 mg and to 30% with the dose of 20 mg, while d-tubocurarine (5 mg) and Pancuronium (1 mg) also significantly mitigated myalgia to become 29% and 28% respectively. Fazadinium even in doses of 15 mg remained relatively ineffective as myalgias were observed in 45% and 33% cases on first and second post-operative day. Moreover, more than 60% cases of difficult intubation were from Fazadinium group.

Ferres, Mirakhur and Craig (1983) compared the influence of d-tubocurarine (5 mg), Gallamine (20 mg), Pancuronium (1 mg) and Vecuronium (1 mg). Each of them was administered either 1 minute or 2 minutes prior to the suxamethonium. Overall frequency of pain was reduced from 41% to 29%. However, precurarization more effectively prevented myalgia on 1st day (16%) when compared to 2nd day (20%). On the analysis of time interval, it was found that all the 1 minute pre-treatment groups had frequency of pain between 19 - 20% except 25% in pancuronium group while pre-treatment with Gallamine, tubocurarine, pancuronium and vecuronium, 2 minute prior to suxamethonium, presented the incidence of 30, 30, 28 and 18.5% respectively. The difference was not significant among the results of different pre-treatment groups. However, the frequency of pain was significantly reduced to 5%, 15% and 10% after pre-treatment with vecuronium (1 minute), vecuronium (2 minute) and Gallamine (1 or 2 minute) group respectively on 1st day, while on 2nd day frequency was reduced to around 10% with tubocurarine (1 minute) and pancuronium as well as vecuronium (2 minutes). Vecuronium was concluded to be most effective. It also abolished severe pains in most of the patients.

The precurarization still remains controversial to impart the protection against the suxa-hyperkalemia. Molecules of a non-depolarizer drug occupy the cholinergic receptors at motor end plate to block the channels in closed state (De Beer, 1959). Thus, they act as a membrane

stabilizing agent to prevent the ionic flux at the time of subsequent suxamethonium administration. Simultaneously the number of available sites, at which suxamethonium may induce depolarization, are reduced leading to the attenuation in the magnitude of the expected potassium efflux (Bali, Dundee, 1975).

Klupp et al (1954), Stevenson (1960), Striker, Morrow (1968), Birtch (1970) and Cooperman (1970) have adequately minimized the hyperkalemic response with the small doses of Gallamine or d-tubocurarine pre-treatment. Gronert Theye (1973) have even succeeded in the abolition of the hyperkalemia with the large doses of the Gallamine pre-treatment.

The d-tubocurarine has been evaluated in the digitalized and the traumatized patients, to show the rise in plasma potassium concentration to become about 50% less than that occurred in non-precurarized patients (Weintraub et al, 1969). The potassium concentrations may be reduced even well below than the pre-induction values and usual fall has been reported to remain between 0.15 m mol/L (Bali, Dundee, 1974) and 0.27 m mol/L (Hukmani et al, 1977).

Konchigeri et al (1975) has obtained potassium concentration to show a maximum fall of 0.31 m mol/L with the Pancuronium (1 mg/kg) pre-treatment. Mean potassium levels were reduced from 3.81 m mol/L (pre-induction) to

3.58 m mol/L (at 2 minutes), 3.66 (at 3 minutes), 3.68 (at 5 minutes), 3.69 (at 10 minutes) and 3.70 m mol/L (at 20 minutes).

Ferres, Mirakhur, Chaig (1983) have administered the Gallamine, Pancuronium, d-tubocurarine and vecuronium either at 1 or 2 minute prior to the injection of suxamethonium. Every regime, but pancuronium (1 minute group) succeeded in reducing the hyperkalemic response. Gallamine (1 minute group) most effectively reduced the potassium levels from 4.08 m mol/L to 3.88 (at 1 minute), 3.80 (at 4 minutes) and 3.96 m mol/L (at 10 minutes), the comparable potassium levels in other groups were as follows :

	Pre-induction	1 mt.	4 mt.	10 mt.
Gallamine (2 mt.)	3.98	3.95	3.88	3.88
Pancuronium (1 mt.)	4.18	4.22	4.15	4.26
Pancuronium (2 mt.)	3.96	3.83	3.81	3.78
Tubocurarine(1 mt.)	3.80	3.85	3.85	3.86
Tubocurarine(2 mt.)	3.80	3.90	3.80	3.90
Vecuronium (1 mt.)	4.23	3.96	3.88	3.96
Vecuronium (2 mt.)	3.93	3.82	3.85	3.80

(All values in m mol/L).

Sullivan et al (1988) also have shown a significant reduction in potassium concentration from 4.0 (pre-induction)

to 3.8 m mol/L (post induction) with the Gallamine and from 4.1 m mol/L to 3.9 m mol/L with the pancuronium (1 mg) pre-treatment.

In contrast to the aforesaid studies, Koide, Waud (1972) have observed a significant rise in potassium level (0.46 m mol/L) even after d-tubocurarine pre-treatment. Basu et al (1973) also have reported definite rise in potassium concentration from 3.86 m mol/L to 4.20 (at 3 minutes), 4.49 (at 7 minutes) and 4.52 m mol/L (at 15 minutes) after similar pre-treatment. Strolting and Peterson (1975) also have concluded precurarization to remain ineffective.

Masey, Glazebrook and Goat (1983) have compared the efficacy of precurarization and self taming. Pre-treatment with 20 mg of Gallamine was found to be superior as fasciculations were seen only in 20% cases in this group while they were present in 56% patients after self taming with suxamethonium 10 mg. Similarly, incidence of myalgia were 44% and 56% in the respective groups, however, muscular relaxation and intubation conditions were far from satisfactory after pre-treatment with Gallamine as onset was delayed from 0.69 minutes to 1.04 minutes and duration of block shortened from 7.6 minutes to 5.23 minutes. Coincidently, it was also observed that pre-treatment dose of suxamethonium itself precipitated fasciculations in 4.8% cases and significant neuro-muscular block in more than 50% of cases.

Sullivan, Williams and Calvey (1988) observed self taming with suxamethonium (10 mg) to remain relatively ineffective when compared to the pre-treatment with Gallamine 20 mg and pancuronium 1 mg. In the self taming group, the median value of fasciculations score was insignificantly reduced from 1.3 to 1.0 while that of myalgia score became 1.7 to 1.4, while Gallamine had significant effect over fasciculations (median score 0.5) and myalgia (0.8). Pancuronium was found to be more effective in prevention of myalgia (0.5) rather than the fasciculations (0.9). Hyperkalemic response to suxamethonium was significantly suppressed by Gallamine. Post-induction plasma potassium concentration was found to be less than that of pre-induction (0.2 m mol/L) while no difference between pre and post induction plasma potassium concentration occurred with the pancuronium and it remained 4.0 m mol/L.

During the course of numerous studies, efforts were and are still on to select most effective drug, dosage schedule and time interval between pre-treatment and suxamethonium. Almost every non-depolarizer but Fazadinium (Bennetts & Khalil, 1981) has been proved to be satisfactory in suppression of fasciculations and myalgia but their effect on hyperkalemic response still needs appropriate confirmation.

Gallamine has remained effective even in very small doses as 5 mg (White, 1962) or 8 mg (Burtles, Tunstall, 1961) even though very large dose of 40 mg Gallamine was suggested

by Davidson (1954). But the consensus is in favour of intermediate dose of 20 mg (Foster, 1960) because larger dose adversely affect the suxamethonium block (Miller & Way, 1971) leading to poor relaxing making intubation difficult (Massey et al, 1983).

Bennike and Neilsen (1964) suggested doses of d-tubocurarine to be administered on body weight basis. Similarly, Wig & Bali (1979) recommended use of Pancuronium in the dose of 0.01 to 0.02 mg/kg. Eroke et al have used d-tubocurarine (0.05 mg/kg), Gallamine (0.25 mg/kg), Pancuronium (0.01 mg/kg), Vecuronium (0.01 mg/kg) and alcuronium (0.03 mg/kg).

Bennetts and Khalil (1981) argued that well perfused lean muscle mass rather than whole body weight would be a more appropriate guide for dose assessment, but obvious difficult to measure. They recommended standard pre-treatment doses such as 10 - 20% of standard equipotent intubation dosages of non-depolarizer. Thus, Gallamine (10 - 20 mg), tubocurarine (5 mg.) and Pancuronium (1 mg.) were suggested and same opinion was put forward by Ferres (1983) and accepted by Masey et al (1983) and Sullivan et al (1988).

Time interval between pre-treatment and suxamethonium too remained variable between 30 seconds (Domaoal et al, 1975) to 4 minutes (Eroke et al, 1983). Although 1 minute interval

(Collin, 1975) and 2 minute interval (Bennett, Khalil, 1981 and Ferres et al, 1983) were also recommended yet 3 minutes schedule remained most acceptable to obtain maximum efficacy of such pre-treatment (Takki et al, 1972; Millar Way, 1971; Wig & Bali, 1979 and Masey et al, 1983).

MATERIAL AND METHODS

MATERIAL AND METHODS

The present study was conducted in the Department of Anaesthesiology in M.L.B. Medical College, Jhansi (U.P.) with the aim to observe the effects of the Self taming, as well as the precurarization, over the suxamethonium induced fasciculations, myalgia and hyperkalemia. The efficacy of both the measures was also evaluated in the prevention of these adverse effects of suxamethonium. The precurarization was performed either with Gallamine or with Pancuronium, so effects of both these drugs were analysed to compare with those of Self Taming.

Eighty indoor patients of either sex between 12 to 55 years comprised the material for the study. All patients undergone general anaesthesia for various types of surgical procedures, in which ambulation in post-operative period was predictable within 24 hours. Such selection was important for better understanding of suxamethonium induced myalgia as they are known to be common during first post-operative day. Obviously, the cases of major abdominal and orthopaedic surgical procedures were excluded from the study. Similarly, patients who might be susceptible for massive hyperkalemic response to suxamethonium were avoided. Thus, patients of burn, neurological disorders, massive muscular trauma, severe

infections and renal failure were not included while selecting the patients.

All the patients were of physical status A.S.A. Grade I or II. They were thoroughly examined pre-operatively to assess the clinical fitness. Routine investigations alongwith relevant special investigations were performed in all the patients and only patients with normal investigation were accepted for the purpose of the study. Written consent was obtained from every selected patients and they were kept empty stomach for at least 6 hours before the induction of anaesthesia.

Premedication consisted of only injection Atropine 0.6 mg I.M. approximately 30 - 45 minutes prior to the induction of anaesthesia. Hyphotic and narcotic analgesics were not administered as they might alter the incidence and severity of myalgia.

Venepuncture was performed aseptically and 5% Dextrose in D/W was started. Care was taken not to infuse only electrolyte containing solution as they might affect the plasma potassium concentrations. Preoxygenation with 100% O_2 was initiated about three minutes prior to the induction of anaesthesia. Induction of anaesthesia was performed with the 2.5% solution of Inj. Thiopentone 5 mg/kg (150-300 mg) intravenously slowly till abolition of eye lash reflex.

Initial anaesthetic management varied as patients were randomly allocated into four separate groups.

Group I (Control group) : Suxamethonium I.V. in dose of 1.5 mg/kg (50-100 mg) was administered as a bolus about 30 seconds after induction with Inj. Thiopentone.

Group II (Self Taming group) : Small dose of suxamethonium (10 mg.) was administered soon after the Inj. Thiopentone, but one minute prior to the full paralysing dose of suxamethonium (1.5 mg/kg.).

Group III (Gallamine group) : Pre-treatment with injection Gallamine 20 mg I.V. was performed 2 minutes prior to the Inj. Thiopentone. The Suxamethonium (1.5 mg/kg) was administered 1 minute after the Inj. Thiopentone so that interval between precurarization and paralysing dose of suxamethonium remained to be 3 minutes.

Group IV (Pancuronium group) : Pre-treatment with Inj. Pancuronium 1 mg I.V. was performed 3 minutes prior to the administration of suxamethonium.

Subsequent management remained same in each group. Endotracheal intubation was performed in every patient as soon as abolition of suxamethonium fasciculation occurred. Connections were made to attach the patient with the Mapleson A circuit of Boyle's Apparatus. I.P.P.V. was continued till recovery from suxa-paralysis was evident.

Subsequently, spontaneous respiration was maintained till completion of the surgical procedure.

Anaesthesia was maintained with the mixture of O_2 + N_2O + Ether. Total gas flow rate was adjusted to remain between 7-9 litres/minute. The ratio of the oxygen and the nitrous oxide was kept to remain 33 : 67.

Besides parameters, stipulated for the present study, each patient was constantly monitored to assess the vital function including pulse, Blood Pressure and respiratory movements.

Fasciculations were observed after administration of suxamethonium to assess their extent and intensity. They were graded as follows :

0 : No visible fasciculations.

+ : Very fine facial muscle and finger tips movements.

++ : Minimal contractions of the trunk and the extremities.

+++ Vigorous contractions of the Trunk and the extremities.

The magnitude of hyperkalemic response to suxamethonium was assessed by the estimation of serum potassium before and after the administration of the drug. Three blood samples were drawn from a separate venepuncture site with the help of dry autoclaved syringes.

1. 5 minutes before administration of Thiopentone.

2. 3 minutes after the Suxamethonium administration.

3. 10 minutes after the Suxamethonium administration.

Blood in each sample was allowed to clot till separation of serum in dry vials occurred. Serum of each vial was separated in different test tubes to be centrifuged for 20 minutes at the rate of 3000 rpm and 0.3 ml of clear serum was obtained for the measurement of serum potassium by the flame photometer.

Principle of the Flame Photometer :

The specimen solution is sprayed as a fine mist into a non-luminous flame which become coloured by characteristic emission of the metal. The first test in the estimation is to prepare a dilution of the specimen to bring the concentration of the element into correct range. Each sample is compared with the standard to eliminate the effects of slow drifts in the sensitivity, which are liable to result from the flame radiation. The whole basis of the method depends on the assumption that a given concentration of the element in the diluted test samples will produce the same amount of light as the same concentration in the standard.

Procedure :

0.2 ml of serum was diluted with 19.8 ml of double distilled water to make the ratio of 1 : 100. This diluted

specimen was compared with standard solutions of potassium chloride, which were made by diluting the stock potassium standard (10 m mol/L = 0.746 of Dry Potassium Chloride/L). Flame photometer was switched on and Potassium filter was inserted. Air pressure was adjusted to 10-16 lb/inch^2 and gas supply was ignited to obtain clear flame without any soot. Subsequently, the various standard solutions were placed in levelled beakers. Initially, high potassium standard (0.08 mEq/L) was sprayed and needle was adjusted to the mark of 100. Zero setting was checked with double distilled water. Each standard was sprayed in turn to confirm the even spraad of the reading over the scale. The diluted specimen sample was spread and reading was noted, it was immediately followed by spraying the two nearest standard solutions which gave readings just higher and lower than unknown sample. After each reading, double distilled water was sprayed to confirm the zero setting and to rule out any error due to remaining potassium.

Assessment of suxa-myalgia was done by visiting the each patient after 24 hours of surgery. Initially, some non-specific enquiry was made regarding the post-operative status of patient. When patient complained about their aches and pains, the sites and severity of pains were recorded. In the cases of negative complaints, the specific quiery was made to ascertain the occurrence of muscle pains and stiffness.

The post-operative pains in the vicinity of surgery and injection sites were not considered as suxa-pains. Low backache in cases who undergone lithotomy position was also not included in the category of suxa-pains.

The intensity of pain was graded as under :

0 : No muscle pain.

+1 : Mild generalized or localized pain.

+2 : Pain at numerous sites/severe pain at a single site.

+3 : Severe pain at numerous sites.

The statistical analysis :

The observations, made during the study, were arranged in tabulated form to obtain the incidences and percentages of the post suxamethonium fasciculations and the post-operative myalgia, as per their intensities in each of the groups. The estimated plasma concentrations were also similarly arranged to express them as the mean values ($\pm$ standard deviation) as to find out any changes, from their respective pre-induction value, at the interval of 3 minutes and 10 minutes after the suxamethonium administration.

The comparative analysis was performed with the help of the following statistical equations.

1. 't' test for the proportionate values :- To compare the incidences of the fasciculations, as well as the myalgias, in between the patients of the control group and each of the pre-treatment group.

$$t = \frac{p_1 - p_2}{\sqrt{pq\left(\frac{1}{n_1} + \frac{1}{n_2}\right)}} \qquad \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots (1)$$

degree of freedom = $|\ (n_1 + n_2) - 2\ |$

where

p_1 = $\dfrac{\text{No. of patients with fasciculations or myalgia}}{\text{Total number of patients}}$ (in the control group).

p_2 = $\dfrac{\text{No. of patients with fasciculations or myalgia}}{\text{Total number of patients}}$ (in pre-treatment group)

n_1 = Total number of patients in control group.

n_2 = Total number of patients in pre-treatment group.

$$p = \frac{p_1\ (n_1-1) + p_2\ (n_2-1)}{(n_1 + n_2) - 2}$$

$q = (1 - p)$

2. Paired 't' test :- To analyse the pattern of the change in the mean plasma potassium concentration, in individual groups, from their pre-induction values.

$$t = \frac{\bar{d}}{sd\ /\sqrt{n}} \qquad \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots (2)$$

degree of freedom = $(n - 1)$

where

$\bar{d}$ = mean of differences of the plasma potassium concentration between the values at

a) Pre-induction and at 3 minutes interval.

b) Pre-induction and at 10 minutes interval.

s.d. = Standard deviation of $\bar{d}$.

n = Number of patients in each group.

't' value, thus obtained from the equation (1) or (2) were utilized to find out the P value which denotes significance of the difference in the value as per under-mentioned criteria.

$P = \nearrow 0.05$: Insignificant.

$P = \angle 0.05$: Significant.

$P = \angle 0.02$: Highly significant.

OBSERVATIONS

OBSERVATIONS

A total number of eighty patients were selected and randomly allocated to the four groups to fulfil the purpose of the present study. Each group was comprised of 20 patients of either sex and physical status A.S.A. grade I and II.

The age of patients was ranging from 12 to 55 yrs and 65% of the patients were of the age between 21 to 40 years.

Table 1

Age distribution of the patients.

Age group	Group I	Group II	Group III	Group IV	Total
10 - 20	3	4	4	3	14
21 - 30	9	10	8	7	34
31 - 40	5	3	4	6	18
41 - 50	2	2	1	2	7
51 - 60	1	1	3	2	7
n =	20	20	20	20	80

The number of the female patients dominated in the model of the present study and the proportion of male and female patients was found to be 42 : 58 (1 : 1.38). Coincidentally the ratio was 1 : 1 in group IV.

Table 2

Sex distribution of the patients.

Groups	Total No.of patients	Male		Female	
		No.	%	No.	%
I	20	9	45%	11	55%
II	20	8	40%	12	60%
III	20	7	35%	13	65%
IV	20	10	50%	10	50%
Total	80	34	42%	46	58%

Fasciculations :

The occurrence of the visible fasciculations was observed soon after the administration of the suxamethonium. The patients in the control group were observed to show highest frequency of fasciculations as each patient in this group (Group I) had fasciculations of the varying intensity. The mild, moderate and severe fasciculations were seen in 55, 25 and 20% of the patients respectively.

Table 3

Incidence of fasciculations.

Groups	Total No.of patients	Patients showing fasciculations	
		No.	%
I	20	20	100%
II	20	5*	25%
III	20	4*	20%
IV	20	10*	50%

* $P = \angle 0.001$ (Significantly different from the control group).

The fasciculations counts were greatly lowered when measure of self taming was employed. Only 25% of the patients in self taming group (Group II) showed fasciculations and those too were of the mild intensity. However, mild fasciculations were also observed in the 20% patients after the self taming dose (10 mg.) of the suxamethonium.

Table 4

Fasciculations with both the dose of the suxamethonium in Self Taming group.

Doses of suxamethonium	Fasciculation grades							
	+		++		+++		Total	
	No.	%	No.	%	No.	%	No.	%
Ist dose (10 mg)	4	20%	-	-	-	-	4	20%
IInd dose (100 mg)	5	25%	-	-	-	-	5	25%

The measure of precurarization was also found to be successful in attenuating the fasciculations. Only 20% cases in Gallamine group (Group III) showed the fasciculations. Severe fasciculations were abolished and frequency of mild and moderate fasciculations were 15 and 5% respectively.

The pancuronium pre-treatment moderately reduced the incidence of fasciculations to 50% in the patients of Group IV. Severe fasciculations could not be abolished as they were seen in one of the total 20 cases. The mild and moderate fasciculation were visible in 40% and 5% patients respectively.

Table 5

Intensity of the fasciculations.

Groups	Total No.of patients	Fasciculations Grades			
		0	+	++	+++
I	20	-	11	5	4
II	20	15	5	0	-
III	20	16	3	1	-
IV	20	10	8	1	1

Table 6

Incidence and intensity of fasciculations (%).

Groups	Fasciculation grades				
	0	+	++	+++	Total
I	0	55	25	20	100
II	75	25	0	0	25
III	80	15	5	0	20
IV	50	40	5	5	50

Myalgia :

The post-operative myalgia were quite common in the patients of the control group. The 65% patients in this group complained about the muscular pains and stiffness in the region of the back of neck, jaw, shoulders, lower chest cage, pectorals and upper abdominal wall. The myalgia remained localized to a single site in 25% patients and it was of mild intensity. The moderate and severe pains were present in 30 and 15% patients respectively. Thus, the frequency of moderate myalgia was found to be highest as they were seen in 46% of the patients who had complained of the after pains.

The patients, in the control group, were also studied to observe the correlationship between the occurrence of the myalgia and the age and sex of the patients. The tendency

to suffer with the myalgia was observed to remain highest in age group 41-50 as myalgia were complained by both the patients in this age group, even the severe pains were present in one of these patients. Susceptibility was observed to be relatively less in the age groups 31-40 and 21-30 years as 80% and 67% of the patients from these age groups respectively had complaints of the after-pains. One patient from each of these three age groups had suffered with the severe after-pains. The incidence of myalgia was observed to be markedly reduced in the patients below 20 years of age and only one of the three patients complained to have mild myalgia. The myalgia were not observed by the patient, having age more than 50 years.

Table 7

Incidence of myalgia in relation to the age of the patients in control group.

Age groups	Total No. of patients	Presence of myalgia		Myalgia grades		
		No.	%	+	++	+++
10 - 20	3	1	33%	1	-	-
21 - 30	9	6	67%	2	3	1
31 - 40	5	4	75%	1	2	1
41 - 50	2	2	100%	-	1	1
51 - 60	1	-	-	-	-	-
Total	20	13	65%	4	6	3

Susceptibility to have myalgia was observed to remain higher in the female patients. 72% of the female patients in the control group complained to have the after-pains, while such pains were present only in 55% of the male patients in the same group. Moreover, the females were more prone to suffer with the severe pains.

Table 8

Incidence of myalgia in relation to the sex of the patients in control group.

Sex	Total No. of patients	Presence of myalgia		Myalgia grades		
		No.	%	+	++	+++
Male	9	5	55%	2	2	1
Female	11	8	73%	2	4	2
Total	20	13	65%	4	6	3

The patients, in the control group, were observed to search out any possible correlationship between the fasciculations and the myalgia, but the observations failed to reveal any definite trend to show the relationship between them.

The myalgia remained absent in 27%, 40% and 50% of the patients who have showed mild, moderate and severe fasciculations respectively, while severe myalgia were complained by the 19% and 25% patients, in which respective intensity of fasciculation was mild and severe. 27% moderate pain occurred in association with mild fasciculation, while 40% and 27% moderate myalgia were associated with the moderate and severe fasciculations respectively.

Table 9

The relationship between the fasciculations and the myalgia.

Fasciculation grades	No.of pts.	Myalgia grades							
		0		+		++		+++	
		No.	%	No.	%	No.	%	No.	%
0	-	-	-	-	-	-	-	-	-
+1	11	3	27%	3	27%	3	27%	2	19%
+2	5	2	40%	1	20%	2	40%	-	-
+3	4	2	50%	-	-	1	25%	1	25%
Total	20	7	35%	4	20%	6	30%	3	15%

The incidence of myalgia could not be reduced when measure of self taming was employed. The considerably higher number of patients in this group had complaints of the myalgia. This incidence of myalgia was found to be 60% which was not significantly different from that in the

control group. Moreover, the occurrence of severe pain was observed in 15% patients in both the groups.

In contrast to the self taming, the pre-treatment with non-depolarizer seemed to be effective in prevention of the suxamethonium induced myalgia. The incidence of myalgia, in the Gallamine group (Group III), was significantly reduced from 65% (Control) to 30% with the abolition of the severe pains. The incidence of mild and moderate pains were observed to be 20% and 10% respectively.

The Pancuronium pre-treatment remained most effective as the incidence of myalgia were greatly reduced to 25% with the abolition of the severe and even moderate pains.

Table 10

Incidence of the Myalgia.

Groups	Total No. of patients	Presence of myalgia	
		No.	%
I	20	13	65%
II	20	12*	60%
III	20	6**	30%
IV	20	5***	25%
Total	80	36	45%

* $P = > 0.3$ Not significantly different from the control group.

** $P = < 0.05$ } Significantly different from the control group.

*** $P = < 0.02$ }

Table 11

Intensity of myalgia.

Groups	Total No. of patients	Myalgia grades			
		0	+	++	+++
I	20	7	4	6	3
II	20	8	6	3	3
III	20	14	4	2	-
IV	20	15	5	-	-

Table 12

Incidence and intensity of myalgia (%)

Groups	Total No. of patients	Presence of myalgia		Myalgia grades		
		No.	%	+	++	+++
I	20	13	65%	20%	30%	15%
II	20	12	60%	30%	15%	15%
III	20	6	30%	20%	10%	-
IV	20	5	25%	25%	-	-

Hyperkalemic response :

The suxamethonium administration, in patients of control group, induced a sustained and significant rise in mean plasma potassium concentration from 3.82 m mol/L (pre-induction) to 4.10 m mol/L and 3.94 m mol/L at 3 and 10 minutes intervals respectively. Thus the mean peak rise of 0.28 m mol/L and 0.12 m mol/L occurred at 3 minutes and 10 minutes interval respectively. The maximum rise in plasma potassium concentration in individual patients were measured to remain within the range of 0.16 m mol/L to 0.34 m mol/L.

This hyperkalemia remained significant even upto the 10 minutes interval after the administration of the suxamethonium. The mean maximum rise of 0.12 m mol/L was observed with the range of 0.08 m mol/L to 0.16 m mol/L.

Table 13

Plasma potassium concentrations (1) Pre-induction - K_1 (2) At 3 minutes - K_2, (3) At 10 minutes - K_3.

Groups	Plasma potassium concentrations (m mol/L)					
	K_1		K_2		K_3	
	Mean value	S.D.	Mean value	S.D.	Mean value	S.D.
I	3.82	±0.13	4.10	±0.17	3.94	±0.14
II	3.93	±0.14	3.75	±0.15	3.80	±0.15
III	3.78	±0.14	3.58	±0.14	3.64	±0.12
IV	3.81	±0.14	3.59	±0.14	3.64	±0.15

The hyperkalemic response was observed to be largely attenuated with the measure of self taming. The patients in this group were having a significant fall in mean plasma potassium concentrations, which was reduced from 3.93 m mol/L (pre-induction) to 3.75 m mol/L at 3 minutes interval. The maximum fall was measured to remain within the range of 0.24 to 0.14 m mol/L with the mean fall of 0.18 m mol/L at 3 minutes after full dose of the suxamethonium administration.

The potassium levels showed the tendency to return towards pre-induction value at the interval of 10 minutes when the mean plasma potassium concentration became 3.80 m mol/L yet it still remained 0.13 m mol/L less than that of pre-induction levels (3.93 m mol/L).

Table 14

Mean change in plasma potassium concentration at 3 minutes ($K_2 - K_1$) and at 10 minutes ($K_3 - K_1$).

Groups	Mean change in P.P.C. (m mol/L)	
	K_2-K_1 ($\pm$ S.D.)	K_3-K_1 ($\pm$ S.D.)
I	+0.28 ($\pm$0.06)	+0.12 ($\pm$ 0.02)
II	-0.18 ($\pm$ 0.03)	-0.13 ($\pm$ 0.01)
III	-0.20 ($\pm$ 0.05)	-0.14 ($\pm$ 0.03)
IV	-0.22 ($\pm$ 0.03)	-0.17 ($\pm$ 0.04)

P.P.C. = Plasma Potassium Concentration.

Table 15

Minimum and maximum change in P.P.C. at 3 and 10 minutes interval.

Groups	Change in P.P.C. (m mol/L)			
	3 mts. interval		10 mts. interval	
	Minimum	Maximum	Minimum	Maximum
I	0.16	0.36	0.08	9.16
II	0.14	0.24	0.10	0.18
III	0.12	0.32	0.08	0.18
IV	0.14	0.28	0.10	0.24

P.P.C. = Plasma Potassium Concentration.

The method of precurarization also remained quite effective in attenuation of the hyperkalemic response to the suxamethonium. The potassium levels of the patients in Gallamine group showed a mean fall of 0.20 m mol/L at 3 minutes interval, when the mean potassium concentration was measured to be reduced to 3.58 m mol/L from the pre-induction value of 3.78 m mol/L. In this group, the maximum fall occurred in the range of 0.32 to 0.14 m mol/L. Similar to the self taming group, the potassium levels showed some rise towards pre-induction values at 10 minutes interval, when the mean plasma potassium concentration were measured to be 3.64 m mol/L, which was still 0.14 m mol/L less than the pre-induction value of 3.78 m mol/L.

Table 16

Overall comparison of the self taming and the precurarization.

Groups	Total No. of patients	Fasciculation				Myalgia			
		Absent		Present		Absent		Present	
		No.	%	No.	%	No.	%	No.	%
I	20	-	-	20	100%	7	35%	13	65%
II	20	15	75%	5	25%	8	40%	12	60%
III	20	16	80%	4	20%	14	70%	6	30%
IV	20	10	50%	10	50%	15	75%	5	25%

Table 17

The change in plasma potassium concentration(P.P.C.) at 3 minutes and 10 minutes after Suxamethonium.

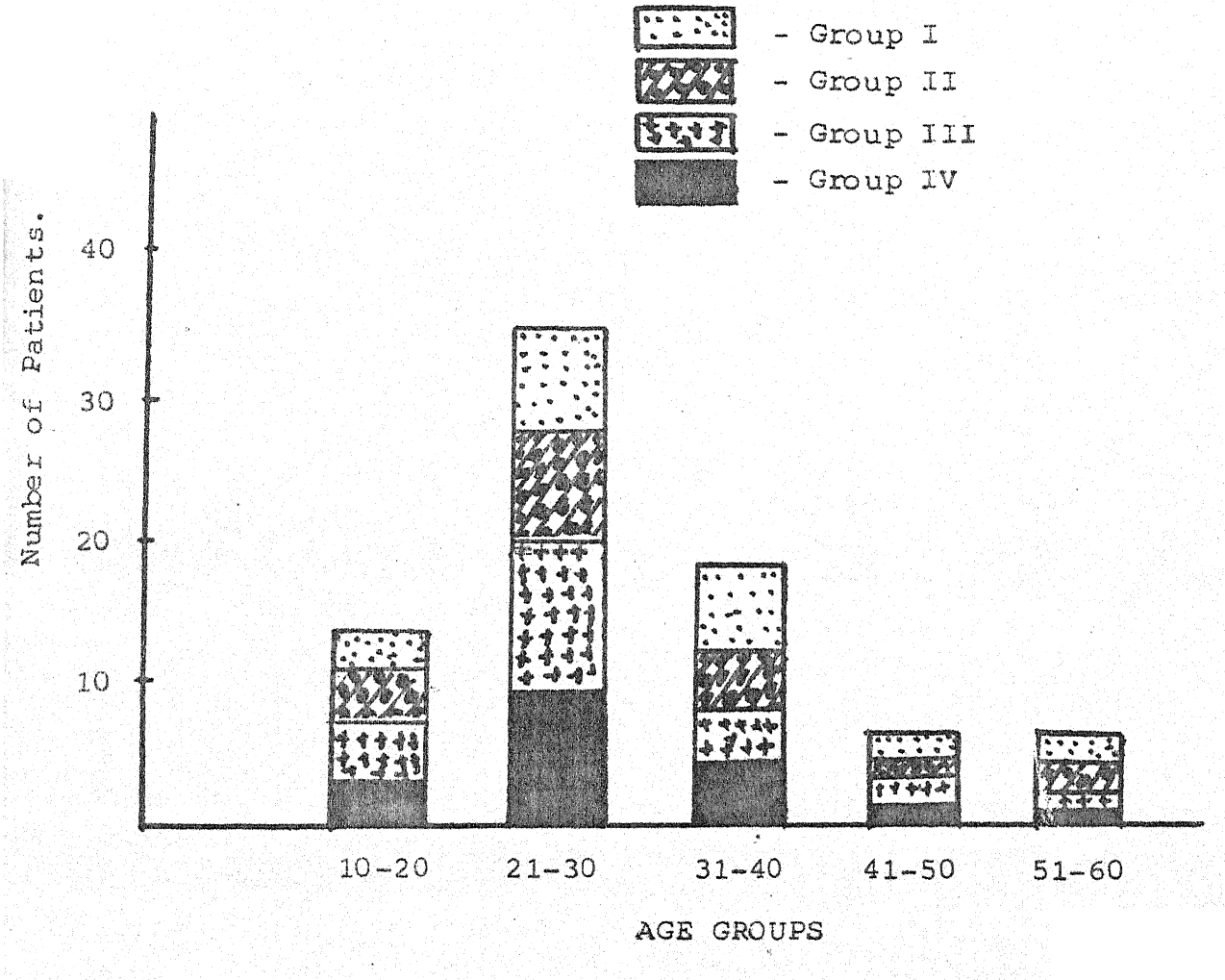
Groups	K_1 (m mol/L)	K_2 (m mol/L)	K_3 (m mol/L)	K_2-K_1 (change in PPC at 3mts.)			K_3-K_1 (change in PPC at 10 mts.		
	Mean(±S.D.)	Mean(±S.D.)	Mean(±S.D.)	Mean(±S.D.)	P value	% change	Mean(±S.D.)	P value	% change
I	3.82(±0.13)	4.10(±0.17)	3.94(±0.14)	+.28(±0.06)	$<$ 0.001	7.3%	+0.12(±0.02)	$<$ 0.001	3.1%
II	3.93(±0.14)	3.75(±0.15)	3.80(±0.15)	-0.18(±0.03)	$<$ 0.001	4.6%	-0.13(±0.01)	$<$ 0.001	3.3%
III	3.78(±0.14)	3.58(±0.14)	3.64(±0.12)	-0.20(±0.05)	$<$ 0.001	5.3%	-0.14(±0.03)	$<$ 0.001	3.7%
IV	3.81(±0.14)	3.59(±0.14)	3.64(±0.15)	-0.22(±0.05)	$<$ 0.001	5.6%	-0.17(±0.04)	$<$ 0.001	4.5%

K_1 : P.P.C. at pre-induction

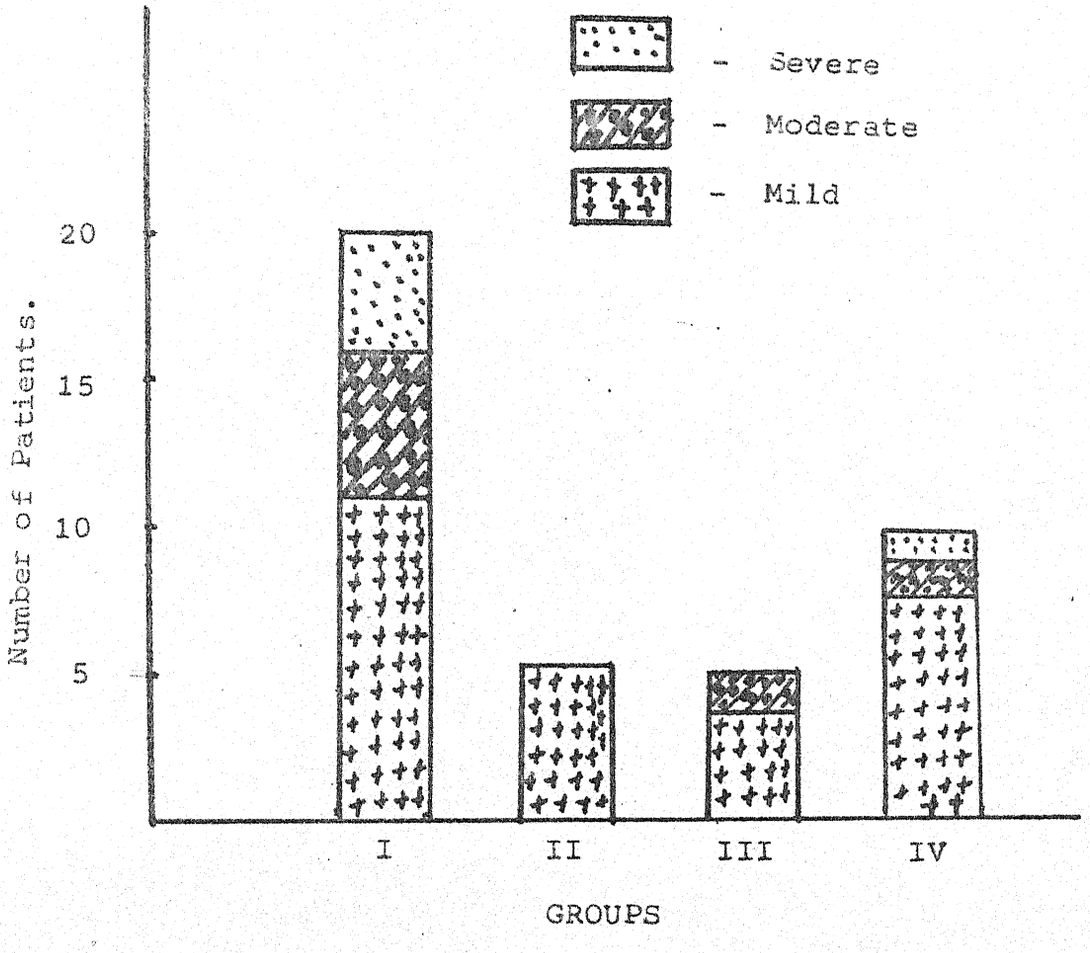
K_2 : P.P.C. at 3 minutes interval

K_3 : P.P.C. at 10 minutes interval.

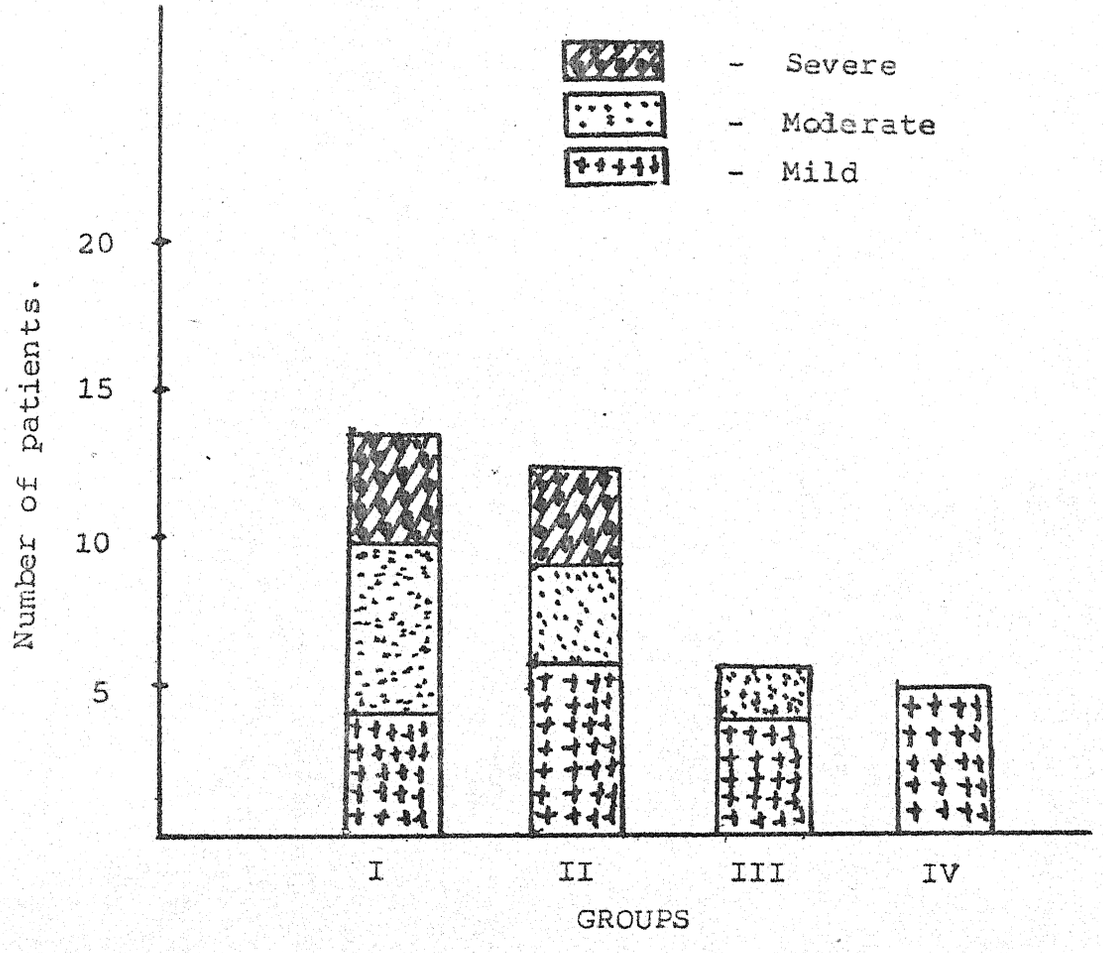
$P = < 0.001$ (in all groups).



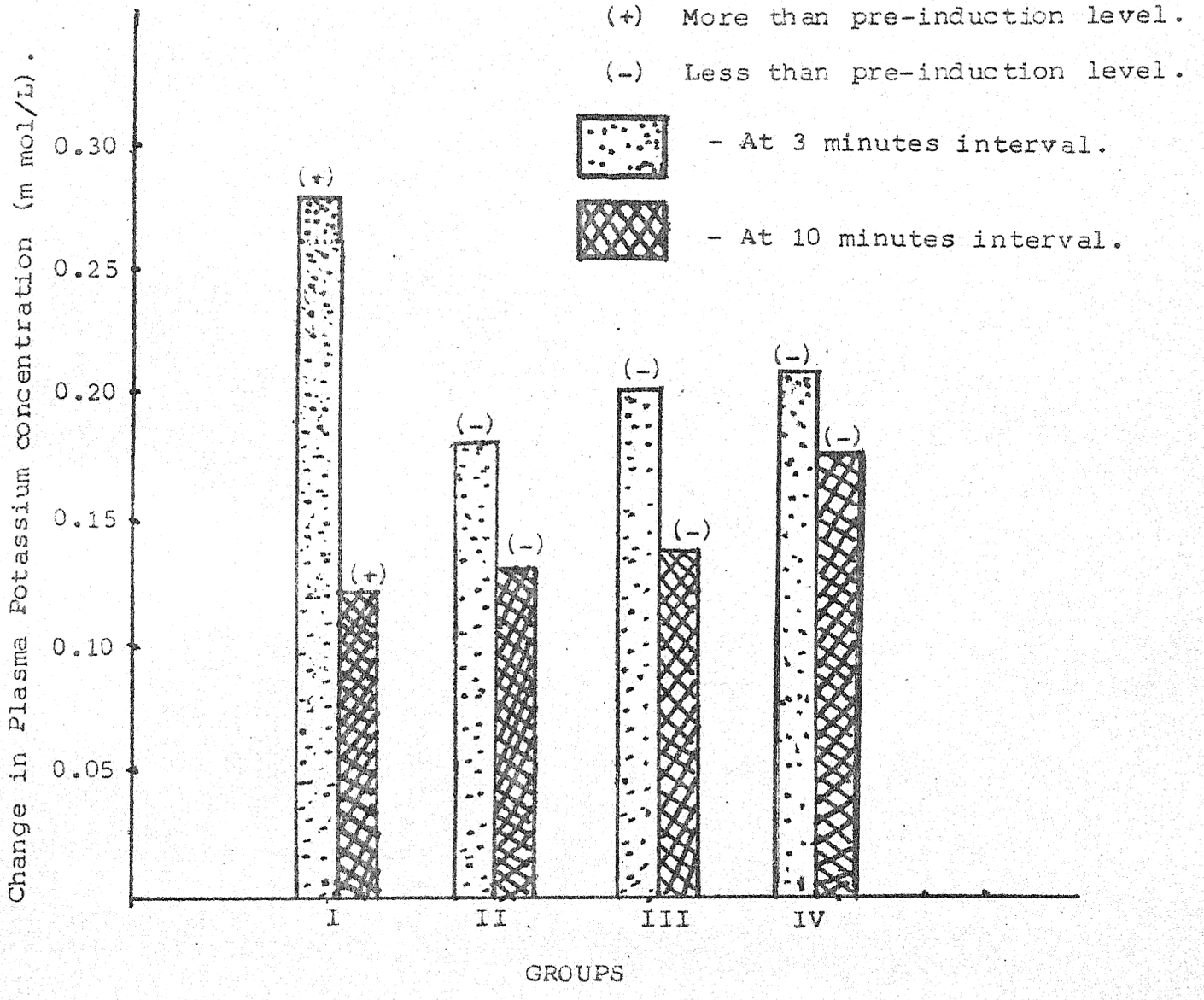
Age distribution of the Patients.



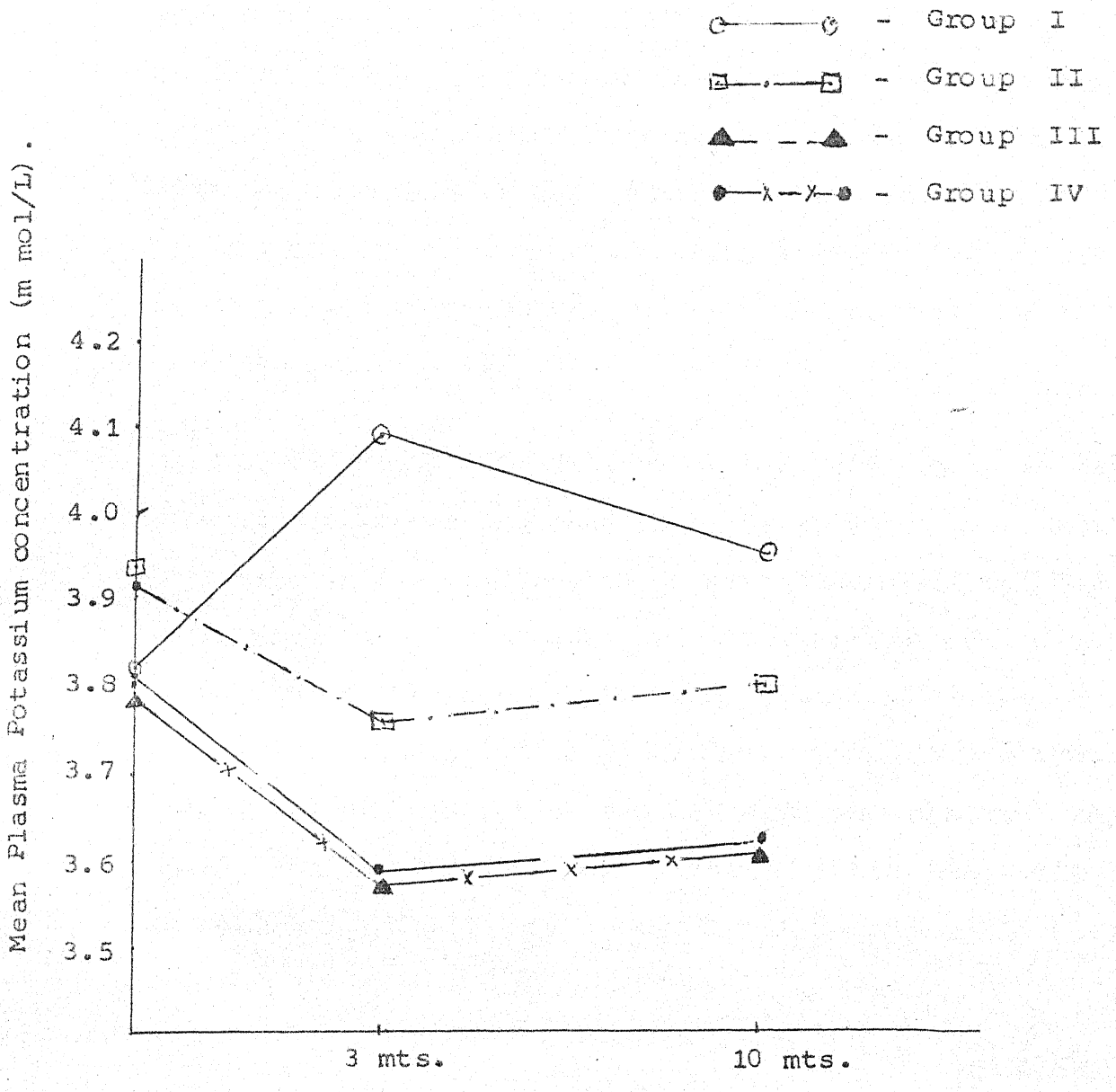
The incidence and intensity of the Fasciculations



The incidence and intensity of the Myalgia



The mean change in the Plasma potassium concentration.



Mean Plasma potassium concentration at the interval of 3 and 10 minutes after the Suxamethonium.

The Pancuronium pre-treatment (Group IV) also effectively lowered the mean plasma potassium concentration from 3.81 m mol/L (Pre-induction) to 3.59 and 3.64 m mol/L at 3 and 10 minutes interval respectively. The maximum fall of 0.28 m mol/L occurred at the 3 minutes interval with the mean fall of 0.22 m mol/L. This fall remained sustained but with the lesser magnitude upto the 10 minutes interval when the mean fall of 0.17 m mol/L were measured, with the range of 0.24 to 0.10 m mol/L.

The overall comparison of the self taming and the precurarization showed that both the measures were equally effective in the suppression of suxa-fasciculations and the suxa hyperkalemia. However, precurarization, either with Gallamine or with Pancuronium also succeeded in the prevention of suxa-myalgia to reduce the incidence from 65% to 30% with Gallamine and 25% with pancuronium. Self taming was not found to be effective in this regard as the incidence of myalgia was insignificantly reduced to remain 60%.

DISCUSSION

DISCUSSION

The suxamethonium, inspite of having property to provide excellent muscular relaxation, has received a criticism from time to time for its potentiality to induce the fasciculations, the hyperkalemia and the myalgia. The initial two of them are known to occur immediately after the use of the drug, while the myalgia can trouble the patient even days after surgery during the late post-operative period.

A numerous attempts has been made to minimize such adverse effects of the suxamethonium. These measures included the changes in salt of the drug, change in mode of administration of the suxamethonium. Pre-treatment with a number of drugs such as xylocain, Dantrolene, Diazepam, Magnisium sulphate, calcium gluconate and vitamin C also has been evaluated with variable success. Recently Lysine acetyl salicylate has been suggested to prevent the suxa-pains (Naquib et al, 1987).

The pre-treatment with small dose of suxamethonium itself (Self Taming) and that of non-depolarizing muscle relaxants (precurarization with the Gallamine and the Pancuronium) has been attempted in the present study to evaluate their efficacy.

Though the Thiopentone has been described to influence the incidence of suxa-pains (Ruddles, 1959; Burtles, Tunstall, 1961; Craig, 1964) and the suxa-hyperkalemia (List, 1967; Bali, Dundee, 1974), it has been used in our study as to obtain the rapid and smooth induction. However, the pre-medicants were avoided as Diazepam is known to affect the suxa-myalgia (Verma et al, 1978).

A number of investigators have suggested various doses of non-depolarizers to be administered for the purpose of the precurarization. In our study, standard dose regime, rather than body weight basis, has been employed. Gallamine was administered in the intermediate dose of 20 mg, which is also suggested by Foster (1960), Bennetts, Khalil (1981) and Sullivan (1988). Pancuronium was used in the dosage of 1 mg, which is reported to be effective without altering the suxamethonium block (Blitt et al, 1981).

The time interval between the precurarization and the administration of the suxamethonium was kept to be 3 minutes, as this schedule has been remained associated with the maximum efficacy of the method (Millar, Way, 1971; Wig, Bali, 1979 and Masey et al, 1983).

The precurarization has been reported to remain associated with the inadequate relaxation and the poor intubation condition (Hodge, 1957) and Foster, 1960). However, no such untoward effects of precurarization were

encountered during the course of our study. Similar absence of poor relaxation has also been shown by Domaoal (1975) and Blitt et al (1981).

The suxamethonium, as a self taming dose, was used in the dose of 10 mg. Similar dose has been used by Baraka (1977) and also suggested by Verma (1978), Wilson, Dundee (1980) and Magee, Gallaghar (1984).

Fasciculations :

The fasciculations are transient un-coordinated muscle movement. They coincide to the initial depolarization of the muscle fibres and perhaps occur as a result of pre-junctional receptor stimulation by the suxamethonium (Kitamura et al, 1981).

The present study shows that the incidence of the fasciculation is quite high in the patients of the control group. Each of the patient in this group had fasciculation. The intensity varied in individual patients and 55, 25 and 25% of the patients have shown mild, moderate and severe fasciculations respectively.

Cullen (1971), Dutta et al (1977), Blitt et al (1981) also have reported occurrance of fasciculation in 100% patients in their studies if no pre-treatment is employed. Gillani et al (1984) have shown similar incidence (100%) and observed mild to moderate fasciculations in 80% of the case while severe fasciculations were present in

rest (20%) of the patients. Naquib et al (1987) also have observed fasciculations in each of the patients and showed the incidence of mild, moderate and severe fasciculation to be 53, 20 and 27% respectively.

Kumar et al (1988) have observed the incidence of fasciculation to be 96%. However, no patient in their series showed severe fasciculations and mild and moderate fasciculations were present in 76% and 20% patients respectively.

The prevention of fasciculation is important as their occurrance in abdominal muscle may provoke a rise in intra-gastric pressure and subsequent regurgitation of gastric contents (Anderson, 1962; Wylie, 1963; La Cour, D. 1969; and Millar, Way 1971). Thus the risk to aspirate such regurgitant material is increased many fold particularly in patients having full stomach and delayed gastric emptying, such as obstetric cases and the patients of intestinal obstruction or having acute trauma.

Similarly, the fasciculation of the extra-ocular muscles may contribute to the rise in intra-ocular pressure which may be dangerous in cases of perforated eye injury and in patients of Glaucoma (Millar, Way, 1971; Meyer et al, 1980).

Initially fasciculations has also been related to the suxa-pains (Davidson, 1954; Bennike Neilsen, 1964) and suxa-hyperkalemia (Klupp et al, 1954; Bali, Dundee, 1975).

but no such relationship could be established by Morris, Dunn (1957), Leatherdale et al (1959), Burtles Tunstall (1961) and White (1962).

The observations of our study confirmed the opinion that the occurrance of the post suxamethonium pains has no correlationship with the incidence and the intensity of the visible fasciculations.

All the patients in the control group of present study, showed fasciculation to be visible but only 65% of them developed suxa-pains in the late post-operative hours. The severe pains occurred in only 25% of the patients who showed severe fasciculations while they were also seen in the 19% of patients who had only minimal fasciculation. Moreover, the myalgia was not complained by 50% of the patients, in which severe fasciculations were seen.

Newnam Loudon (1966) have shown even the absence of the myalgia in the patients in which severe fasciculations were seen while the incidence of myalgia was more than 55% among the patients, showing only minimal fasciculations. Collier (1975), Magee et al (1977); Bennett, Khalil (1981), Ferres (1983) and Gillani et al (1984) supported the view that incidence and intensity of the fasciculation have no effect over the occurrance of myalgia.

The absence of this relationship has also been strengthened by the observations in the Self Taming group of our study, the pre-treatment with small dose of suxamethonium

resulted into significant attenuation of the fasciculation but the occurrance of the suxa-pains remained unaffected.

The present study proves the efficacy of the self taming and the precurarization in the prevention of suxa-fasciculations.

The Self Taming reduced the incidence of fasiculation from 100% to 25% with the abolition of severe and even moderate fasciculations. However, the fasciculations of mild intensity occurred in 20% patients after the self taming dose of suxamethonium.

Similar findings were observed by Baraka (1977) who has succeded, with the measure of Self Taming, in reducing the incidence and intensity of fasciculation from 100% to 20%. Coincidentally, mild fasciculations were present in similar number of patients (20%) after the Ist dose (10 mg.) of suxamethonium. Verma, R.S. et al (1979) have shown the reduction in the incidence of fasciculation with the pre-treatment dose (10 mg.) of suxamethonium. The fasciculation were visible in 52% patients after the Ist dose, while they were largely inhibited and present only in 4% cases after the full dose (100 mg) of suxamethonium. Brodsky et al (1979), Wilson, Dundee (1980), Gillani et al (1984) also have effectively attenuated the suxa-fasciculations with the measure of self taming.

The precurarization with the Gallamine (20 mg, 3 minutes prior to the suxamethonium) has been found, in

present study, to be most effective in the attenuation of the suxa-fasciculations. The fasciculations were greatly inhibited to be visible only in 20% patients. The fasciculations of the mild and moderate intensity were present in 15 and 5% patients respectively, while no patient had severe fasciculations.

The precurarization with the pancuronium (1 mg, 3 minutes prior to suxamethonium), in the present study, was observed to be least effective when compared with the results obtained in Group II (Self Taming Group) and Group III (Gallamine group). The pancuronium could reduce the incidence of fasciculation to remain 50%.

Cullen (1971) has proved the efficacy of Gallamine and pancuronium and d-tubocurarine in the inhibition of suxa-fasciculations. Gallamine (20 mg. 3 minutes prior to the suxamethonium - 1 mg/kg.) was found to be most effective, as none of the patient showed fasciculations. Virtue et al (1975) have shown that Gallamine (20 mg, 30 seconds prior to suxamethonium) can reduce the incidence of fasciculations from 82 to 12%. The incidence were further reduced to only 2% when the Gallamine was used in the dose of 30 mg and administered 60 seconds prior to the suxamethonium. Blitt et al (1981) also have found the Gallamine to be superior than pancuronium. The fasciculations were completely abolished after the Gallamine pre-treatment while the incidence of 30% was observed after the pancuronium.

Myalgia :

The post-operative suxa-pains are most troublesome to the patients and perhaps occur due to muscle damage, induced by the suxamethonium (Collier, 1978). The prevention of such pains is most desirable not only on humanitarian ground but also to fulfil the ethics of discipline of the anaesthesiology.

The present study has shown that occurrance of suxa-pains are quite common. The 65% of the patients in the control group of study were troubled due to presence of post-operative myalgia. The severe pains were also not uncommon, as 15% patients had incapacitating pains.

The similar high incidence of pain also has been reported to be 66% by C. Davidson (1954), 60% by Foster (1960) and 66% by Wilson, Dundee (1980). Even much higher frequency of pains have been shown by Burtles et al (1961) and Mayrhofer (1959) when the incidence of myalgia were 75% and 89% in the respective studies.

In fact the incidence are quite variable and lower incidence of myalgia such as 1.2% (Crawford, 1971), 17% (Craig, 1964) and 25% (Hegar, 1956) also have been reported. Haldia et al (1975) have shown this incidence to be 52% while Magee et al (1987) have observed it to 57%.

The wide range of occurrance of the myalgia seems to be due to the influence of multiple factors which include

the age of the patient (Bush, Roth, 1961), sex of the patient (Leatherdale et al, 1959), pregnancy (Crawford, 1971), muscular fitness of the patient (Newnam, Loudon, 1966), premedication such as Diazepam (Verma et al, 1978) induction agent (Craig, 1964), mode of administration of suxamethonium (Burtles Tunstall, 1961; Craig, 1964), the duration of ambulation (Davidson, 1954) and the position and nature of surgery. Obviously, the standardization of all the aforesaid variables can not be made in a single experimental model.

The observations of the present study suggested that myalgia tend to occur commonly at the site of neck, jaw, shoulder, anterior chest wall, lower costal margins and the upper abdominal wall.

Burtles, Tunstall (1961), White (1962) and Bryson Ormston (1962) have reported the neck, shoulder, pectorals and the lower chest cage to be the common sites at which myalgia occurs. Collier (1978) have suggested that muscles of back of the neck and the lower thoracic cage, owing to have high spindle count, are more liable for the suxamethonium induced muscle damage which make these muscle to be more susceptible to develop the after-pains.

Parbrook and Pierce (1960) and Craig (1964) have observed a relatively high frequency of post-operative low backache. However, in the present study, the low backache was not considered as suxa-pains, for many of the patients

were placed in Lithotomy position, which may itself be a causative factor to produce backache.

Our observations revealed that patients of more than 20 years but below 50 years are much prone to develop the myalgia. The patients in control group have shown the myalgia with the incidence of 67%, 75% and 100% in the age groups of 21-30, 31-40 and 41-50 years respectively.

The influence of age over the occurrance of myalgia is well knewn (Bush, Roth, 1961; Burtles, Tunstall, 1961). Craig (1964) has found the incidence of 13% in the patients below 20 years and 20% in the patients of 31 - 40 years. No myalgia occurred in the patients of more than 50 years of age. The overall low incidence (17%) might be, because suxamethonium was administered only in the dose of 25 mg.

The higher susceptibility to have suxa-pains, in the patients of more than 20 years and below 50 years, also has been described by Burtles, Tunstall (1961). The incidence of myalgia in such patients were observed to remain around 68%.

The children and patients of more than 50 years of age have been shown to be much less prone to have myalgia (Bush, Roth, 1961). The children remain quite active, thus their muscular fitness prevents them from the suxa-pains (Newnam, Loudon, 1966) moreover their muscle tissue contains higher proportion of elastic collagen fibres which minimize the suxamethonium induced muscle damage and so subsequent after-pains (Thind Bryson, 1983).

The female patients, in the control group of the present study, had higher tendency to suffer with the suxa-pains to show the incidence of 72%, while the incidence of 55% was observed among the male patients.

The higher susceptibility of the female patients has also been described by Leatherdale et al (1960), Riding (1975) and Magee et al (1987). Burtles Tunstall (1961) have observed, the myalgia to occur in 59% of the female patients. The male patients were shown to be less prone as they showed the incidence of myalgia to be 49%. Newnam, Loudon (1966) have reported higher incidence of myalgia to be 30% in female patients when compared to that of 13% in the male patients. The reason of higher tendengy of the female patients to develop myalgia is not known, perhaps the hormonal influence may be a causative factor.

Our observations with the Self Taming were found to be dissatisfactory in the prevention of myalgia, 60% patients in this group suffered with suxa-pains and moreover the severe pains were complained by equivalent number of patients (15%) when compared with those occurred in patients of control group.

Our observations well correlated with those of Wilson, Dundee (1980) who have also not succeeded in the prevention of suxa-pains with the help of the Self Taming, as quite high incidence of myalgia was observed, which was 66% in control group and 67% in patients of Self Taming Group.

Brodsky et al (1979) also have reported the incidence of myalgia to remain unaltered whether the Self Taming was employed or not and 25% patients suffered with myalgia with or without the measure of Self Taming. Earlier, Burtles et al (1961) also have failed to reduce the incidence of myalgia with the pre-treatment dose (5 mg.) of the suxamethonium.

In contrast to the most of the studies, Gillani, Dar and Kangoo (1984) have described the Self Taming to remain effective in reducing the incidence of myalgia from 56% to 24% with the abolition of the severe pains.

In view of our observations, alongwith those of others, it seems that the measure of Self Taming has no efficacy against the suxa-pains although it can successful attenuate the occurrance of the fasciculations. Thus, it also becomes evident that the incidence and intensity of the fasciculations has no effect over the occurrence of the suxa-myalgia.

The present study shows that the measure of precurarization is much more purposeful than the Self Taming in the inhibition of the suxamethonium induced adverse effects.

The precurarization with the 20 mg of Gallamine (3 minutes prior to the suxamethonium) significantly reduced the incidence of fasciculation to 20% and that of

myalgia to 30%. No patient in this group suffered with the severe fasciculation or complained to have severe after-pains.

The precurarization with the pancuronium 1 mg (3 minutes prior to the suxamethonium) was found to be even much more effective in regards to reduce the incidence of myalgia to 25%. The severe and, even, the moderate pains were abolished in the pancuronium group of the present study.

The Gallamine pre-treatment has been concluded, in numerous studies, to remain highly effective against the occurrence of the suxa-myalgia. Davidson (1954) has used this drug in the dose of 40 mg to show the successful reduction in the incidence of myalgia from 66 to 40%. White (1962) has significantly reduced the incidence of myalgia from 50 to 29% even when the lower dose (5 mg.) of Gallamine was administered.

Bennetts and Khalil (1981) have also succeeded, with the Gallamine (10 mg.), in the prevention of myalgia to reduce the incidence of suxa-pains from 68 to 33%. The incidence was further lowered to 30% when the 20 mg of Gallamine was used.

Ferres, Mirakhur and Craig (1983) have proved the efficacy of the Gallamine pre-treatment. The incidence of myalgia were lowered from 41% to 30% when the precurarization was performed 2 minutes prior to the suxamethonium. Masey et al (1983) and Sullivan (1988) also have concluded that

the Gallamine (20 mg) pre-treatment remains superior, when compared to the Self Taming, in the prevention of the myalgia.

The results, with the pancuronium, have remained quite variable in the various studies. Brodsky, Brock-utne and Samuels (1979) have found it more effective in the prevention of fasciculations although incidence of myalgia were also reduced from 35% to 20%. Moderate efficacy of the drug has also shown by Suma et al (1979) and Wig, Bali (1979). Casey, Blitt and Carlson (1981) have found it to be superior than Gallamine, d-tubocurarine and metacurine in regard to provide adequate relaxation alongwith effective prevention of the suxa-pains.

Bennetts, Khalil (1981) have got success, with the pancuronium (1 mg.) pre-treatment, in the significant reduction of suxa-myalgia from 68% to 28%. Ferres et al (1983) have used the pancuronium (1 mg.) either at 1 or 2 minutes prior to suxamethonium and the incidence of myalgia were reduced from 41% to 25% and 28% respectively.

Sullivan, William and Calvey (1988) have found pancuronium to be superior as much lower incidence of myalgia (median score 0.5) were found in pancuronium group while the Gallamine group showed the median score of myalgia to remain 0.8.

Hyperkalemia :

All the patients in the control group of our study had definite rise in their mean plasma potassium concentration from 3.82 m mol/L to 4.10 m mol/L to show the mean rise of 0.28 m mol/L at 3 minute interval. The potassium level remained higher even upto 10 minutes, when the mean rise of 0.12 m mol/L was observed. The maximum rise, in plasma potassium concentration, of 0.36 and 0.16 m mol/L occurred at 3 minutes and 10 minutes interval respectively.

The mild and transient rise in the potassium concentration, in response to the suxamethonium, has been shown by Klupp et al (1954), Paton et al (1956), List (1967), Striker Morrow (1968), Bali, Dundee (1974), Magee et al (1984), Naquib et al (1987) and Kumar et al (1987). Mazze et al (1969) have shown a mean rise in plasma potassium concentration, of 0.4 m mol/L, 0.3 m mol/L and 0.2 m mol/L at the respective time interval of 3, 5 and 10 minutes. Miller et al (1972) have measured the potassium levels to show the mean rise of 0.3 and 0.1 m mol/L at 5 and 10 minutes intervals respectively. Konchigeri et al (1975) have described the potassium level to show the mean rise of 0.43 m mol/L at 2 minutes, 0.2 m mol/L at 3 minutes, 0.11 m mol/L at 5 minutes and 0.08 m mol/L at 15 minutes.

Millar et al (1972), Bali, Dundee (1974), Thatte et al (1981) have shown persistance of hyperkalemia upto 10 minutes. However, Mazze et al (1969), Konchigeri et al

(1976) have shown that such response may be sustained for even upto 15 minutes.

The present study shows that both the measures, the Self Taming and the precurarization, are highly efficient in minimizing the hyperkalemic response to the suxamethonium. The mean plasma potassium concentrations can be reduced, with these measures, even upto the extent to remain well below the pre-induction values for at least upto the 10 minutes, after the suxamethonium administration.

The efficacy of Self Taming was observed, in present study, when potassium concentration showed a mean fall of 0.18 m mol/L and 0.13 m mol/L at 3 and 10 minutes interval respectively. The maximum fall of 0.24 m mol/L and 0.18 m mol/L were found at the respective time interval.

The Self Taming also has been evaluated by Thatte, Mulay and Deshpande (1981) to conclude that this measure is quite effective in the prevention of the rise in potassium concentration. The mean fall of 0.3 m mol/L was observed at the interval of 3 minutes, while the mean fall of 0.2 m mol/L persisted from 5 to 10 minutes.

The efficacy of Self Taming has also been shown by Magee, Gallaghar (1984). The mean fall in the plasma potassium concentrations, was measured to be of 0.22 m mol/L, 0.20 m mol/L and 0.23 m mol/L at the respective time interval of 2, 3 and 5 minutes. The maximum mean fall of 0.25 m mol/L occurred at the interval of 6 minutes.

Sullivan et al (1988), however, have observed no changes in the mean potassium concentration from the value of 4.00 m mol/L when the measure of Self Taming was employed.

The observations in the present study suggests that the precurarization either with the Gallamine or with the pancuronium can attenuate the suxa-hyperkalemia upto the significant extent.

The patients in the Gallamine group of the present study were showing the mean potassium concentration to have a fall of 0.20 m mol/L at 3 minutes interval and 0.14 m mol/L at 10 minutes interval. The maximum fall of 0.32 m mol/L and 0.18 m mol/L occurred at the respective interval of 3 and 10 minutes.

The pancuronium pre-treatment was also found to be equally effective in this regard. The patients in this group showed the mean potassium concentrations to have a fall of 0.22 and 0.17 m mol/L at the interval of 3 and 10 minutes respectively. The maximum fall of 0.28 and 0.10 m mol/L were shown by the patients at these respective time intervals.

The efficacy of the Gallamine, in minimizing the suxa-hyperkalemia, has been shown by Klupp et al (1954), Striker, Morrow (1968), Birtch (1970), Cooperman (1970) and Gronert Theye (1973). Ferres et al (1983) have succeeded, with the Gallamine (20 mg 1 minute prior to the suxamethonium), in reducing the potassium concentration to show a mean fall of

0.28 m mol/L at the interval of 4 minutes and of 0.12 m mol/L at the interval of 10 minutes.

The efficacy of the pancuronium has been shown by Konchigeri et al (1975) who observed a maximum fall of 0.31 m mol/L in the potassium concentration after this pre-treatment. A mean fall of 0.23, 0.15, 0.12 and 0.11 m mol/L was observed to be present at the respective interval of 2, 5, 10 and 15 minutes. Ferres et al (1983) have reported that the pancuronium pre-treatment (1 mg 2 minutes prior to the suxamethonium) could reduce the mean potassium concentration to show a mean fall of 0.15 and 0.18 m mol/L at the intervals of 4 and 10 minutes respectively. Coincidentally, the efficacy of this pre-treatment was lowered if the pancuronium was administered only 1 minute prior to the suxamethonium. Sullivan et al (1988) have succeeded to show a mean fall of 0.2 m mol/L in the potassium concentration after pre-treatment either with the Gallamine or with the pancuronium.

Koide, Waud (1972), Basu et al (1973) and Stoelting, Peterson (1975), however, have found the precurarization to remain ineffective in the prevention of the suxa-hyperkalemia.

The overall review of the present study suggest that the Self Taming can efficiently prevent the suxa-fasciculation and the suxa-hyperkalemia. However, it has no significant effect over the occurrence of the myalgia. Baraka (1977) has suggested that either neuro-muscular

accommodation or desensitation of motor end occur with the preliminary dose of the suxamethonium. Thus, the magnitude of the depolarization after the subsequent full dose of the suxamethonium is minimized leading to reduction in the occurrence of the fasciculation and the hyperkalemia.

The precurarization seems to be more effective than Self Taming in regards to reduce the myalgia in the significant manner. The pancuronium more effectively prevented the myalgia then the fasciculations to reduce the incidence of myalgia from 65% to 25%, but the fasciculation were still visible in 50% patients. The Gallamine had more pronounced effect in regards to prevent the fasciculations, as they remained visible only in 20% cases. However, the Gallamine and the Pancuronium showed almost equal efficacy in attenuation of the hyperkalemic response to suxamethonium.

CONCLUSION

CONCLUSION

The analysis of the observations in the present study shows that the occurrence of the post suxamethonium fasciculations and post-operative myalgia is quite high and the suxamethonium certainly induces a definite hyperkalemia, in significant manner, to persist upto 10 minutes.

The fasciculations occurred inevitably as to remain visible in each of the patient in control group. The successful suppression of these fasciculations can be obtained either with Self Taming of suxamethonium or with precurarization by using small doses of Gallamine as well as the Pancuronium. All these measures are significantly effective ($P < 0.001$) in the inhibition of the incidence and intensity of the fasciculations. However, the Gallamine pre-treatment is most superior, in this regards, followed by the measure of Self Taming and then the Pancuronium pre-treatment.

The overall incidence of post-operative suxa-pains also use to remain distressingly high in the non pre-treated patients. Coincidentally, the patients within the range of 21 - 50 years of age and particularly the females are highly susceptible to suffer with such after-pains. However, the

development of these pains has no relations with the incidence and intensity of the post suxamethonium fasciculations. The measure of Self Taming remains ineffective in the attenuation of these after-pains and incidence use to remain largely unaltered ($P > 0.3$). The pre-treatment with the pancuronium has the highest efficacy to mitigate the incidence and intensity of the myalgia ($P < 0.02$). However, the Gallamine pre-treatment is also adequately effective in significant inhibition of the suxa-myalgia ($P < 0.05$).

The post-suxamethonium hyperkalemia is also an inevitable phenomenon. The plasma potassium concentration tends to rise significantly more than pre-induction level for atleast upto the 10 minutes ($P < 0.001$). This response to suxamethonium can, largely, be inhibited by the measure of the Self Taming as well as the precurarization (Pancuronium and Gallamine) to lower the potassium concentration significantly less than pre-induction level ($P < 0.001$).

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S U M M A R Y

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The suxamethonium chloride is one of the most essential drugs, required during the common anaesthetic practice and is almost invariably administered to fascilitate the endotracheal intubation. It is also considered as the relaxant of choice for various short surgical procedures and modified electro-convulsive therapy because of its property to provide excellent muscle relaxation of rapid onset (10-30 seconds) and short duration (1-5 minutes).

The drug is chemically related to the acetylcholine and acts as agonist over the neuro-muscular junction, to block the post-junctional receptors in open state. Thus, weak but relatively persistant depolarization is produced at motor end plate, which becomes unresponsive to further stimuli and complete muscular paralysis is resulted.

This agonistic activity of suxamethonium can also induce certain adverse effects like development of bradycardia, bronchospasm, fasciculations, hyperkalemia, rise in serum creatinine phosphokinase activity, myo-globinuria, rise in intragastric and intra-ocular pressures and occurrence of post-operative myalgia.

Model of Present Study :

The present study was planned with the aims to evaluate the effects of self taming and precurarization over the post-suxamethonium fasciculations, hyperkalemia and post-operative myalgia. A total number of eighty patients, of either sex and between 12-55 years of age, were selected to fulfil the purpose of study. All the patients were of physical status ASA Grade either I or II and they were randomly allocated to four groups, which were as follows : (1) Group I (Control group), (2) Group II (Self Taming Group), (3) Group III (Gallamine group) and (4) Group IV (Pancuronium group).

Self Taming :

Suxamethonium itself was used, in the low doses (10 mg), as a pre-treatment measure. This small dose was administered just after thiopentone but one minute prior to the full paralysing dose of suxamethonium (50 - 100 mg).

Precurarisation :

The Gallamine (20 mg.) or Pancuronium (1 mg.) was administered as a pre-treatment in the respective Groups III and Group IV. Either of these two non-depolarisers was given about 3 minutes prior to the full paralysing dose of suxamethonium.

Anaesthetic management :

Besides the pre-treatment measure, the anaesthetic management remained same in patients of all the study groups. The pre-medication was given only in the form of Atropine 0.6 mg I.M. (30 - 45 minutes prior to the induction). Hypnotic and narotic analgesic were avoided, as Diazepam is known to affect the suxa-myalgia (Verma, 1978). Induction was performed with the thiopentone 0.5 mg/kg (150 mg - 300 mg) followed by the administration of suxamethonium (50 - 100 mg). Subsequently, endotracheal intubation was done and anaesthesia was maintained with the mixture of O_2 + N_2O + Ether (O_2 : N_2O :: 33 : 67 and total gas flow 7 - 9 Lt./mt.).

Observations and Analysis :

The patients in all the groups were observed for the presence of visible fasciculation and three blood samples were drawn to measure the plasma potassium concentration (1) pre-induction, (2) 3 minutes after suxamethonium, (3) 10 minutes after the suxamethonium. The post-operative suxa-myalgia were assessed by visiting the patients 24 hours after completion of surgical procedure. The pain in the vicinity of the surgery, sites of intra-muscular injections and low backache were not considered as suxa-myalgia.

Fasciculations :

The post-suxamethonium fasciculations occur as transient visible muscular twitches, soon after the administration of the suxamethonium, probably because of pre-junctional receptor stimulation by the drug (Kitamura et al, 1981). They tend to subside as soon as the muscular paralysis is developed. However, their presence may fatally lead to the rise in intra-gastric and intra-ocular pressures (Millar et al, 1971) and may potentiate the subsequent hyperkalemic response (Collier, 1978).

The present study shows the quite high incidence (100%) of fasciculation in the patients of control group and severe fasciculations were visible in 20% cases, in which vigorous contractions of trunk and extremities were present.

The Self Taming of suxamethonium reduced the incidence to become only 25% ($P = < 0.001$) with the abolition of the fasciculation of severe intensity. However, Self Taming dose of suxamethonium itself induced mild fasciculations in 20% cases.

The Gallamine pre-treatment also successfully reduced the incidence to 20% ($P = < 0.001$). However, precurarisation with pancuronium was found to be least effective in this regard and fasciculations were present in 50% of the patients in this group ($P = < 0.001$).

Post-operative Myalgia :

The suxa-myalgia use to mimik the muscle pains and stiffness, occuring after the vigorous exercise of the unaccustomed muscle (Leatherdale et al, 1959). They are usually felt within 24 to 48 hours (Parbrook et al, 1960; Haldin et al, 1961) and may persist upto 3 days (White, 1962) or occasionally upto 6 days (Burtles, 1961). Numerous mechanisms have been suggested for the occurrence of such pains and the most probable cause seems to be the muscular injury produced by the suxamethonium (Tommisto et al, 1967; Water et al, 1971 and Collier, 1978).

65% of the patients, in the control group of present study, complained about such pains, which occurred commonly at the site of neck, jaw, shoulders, lower chest cage and upper abdominal wall. Mild, moderate and severe pains were present in 20%, 30% and 15% of the patients in this group. Higher susceptibility to such pains was observed in the patients having the age between 21 to 50 years. Female patients were more prone as 73% of female and 55% of the male patients developed the suxa-pains. However, the myalgia were found to have no relation with the occurrence of the visible fasciculations. The myalgia of severe intensity were felt even in association with minimal fasciculation, moreover no myalgia occurred in 50% of patients who had severe fasciculations.

The Self Taming of suxamethonium was found to be ineffective in the prevention of myalgia, as the incidence remained to be 60%, which was not significantly different from that in the control group ($P = \nabla 0.3$). Moreover, similar number of patients (15%) complained of the severe myalgia in both the groups.

Precurarization with Gallamine significantly reduced the incidence to 30% ($P = \angle 0.05$) with the abolition of severe pains. The pancuronium pre-treatment most effectively reduced the incidence to 20% ($P = \angle 0.02$) with the abolition of severe and even moderate pains.

Hyperkalemia :

Hyperkalemic response to the suxamethonium is a dose dependent phenomenon (Klupp et al, 1954) and reflected as mild rise in plasma potassium concentration from the pre-induction value (Paton, 1956; List 1967; Bali, Dundee, 1974). Muscle tissue acts as the source of the potassium (Paton, 1954; Bali et al, 1974). The potassium is released during the process of depolarization at the motor end plate (Gronert et al, 1975) and fasciculations may potentiate this release (Roth, 1969; Collier, 1978). This hyperkalemic response remains clinically insignificant in healthy patients but may lead to the fatal ventricular arrythmia in the cases of burns (Allen et al, 1961; Tolmie et al, 1967), Tetanus (Roth et al, 1969), Massive trauma (Manze et al, 1969),

Renal failure (Roth et al, 1969; Powell et al, 1970) and the patients of upper and lower motor neuron disorders (Gronert et al, 1975).

The definite and sustained hyperkalemia was shown by all the patients in the control group of present study. The mean rise of 0.28 m mol/L and 0.12 m mol/L occurred in the mean plasma potassium concentration, at the respective time interval of 3 and 10 minutes after the suxamethonium ($P = \leq 0.001$).

The hyperkalemic response was largely attenuated by all the three pre-treatment measures, employed in present study. The mean plasma potassium concentration were significantly lowered to become even less than pre-induction values. The Self Taming of suxamethonium caused a mean fall of 0.18 m mol/L at 3 minutes and of 0.13 m mol/L at 10 minutes interval ($P = \leq 0.001$). The Gallamine pre-treatment was resulted into mean fall of 0.20 m mol/L and 0.14 m mol/L at these respective time intervals ($P = \leq 0.001$). Similarly, the pancuronium pre-treatment was associated with the significant reduction in the potassium concentration to show the mean fall of 0.22 m mol/L and 0.17 m mol/L at 3 minutes and 10 minutes interval respectively ($P = \leq 0.001$).

The overall review of the present study suggest that the Self Taming of suxamethonium can effectively reduce the muscle fasciculation and the hyperkalemic

response, however, it hardly has any influence over the post-operative myalgia. The precurarization either with the Gallamine or with the Pancuronium may be considered a better choice as it is capable to minimise the suxamyalgia too. However, the Gallamine has more pronounced effect against the fasciculation while the pancuronium is much more effective in the prevention of the suxamyalgia. The efficacy of all the measures remains statistically similar in regards to attenuate the hyperkalemic response.
